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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: SABIHA QAZI Examiner #: 74141 Date: 3/4/03
Art Unit: 1616 Phone Number 305-3910 Serial Number: 10/022,138
Mail Box and Bldg/Room Location: 2D19, 3B07 Results Format Preferred (circle): PAPER DISK E-MAIL

If mor than one search is submitted, please prioritize searches in order of need. mej

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Steroid Hormone Products + methods for preparing them.

Inventors (please provide full names): THOMAS SCHULTZ.

Earliest Priority Filing Date: 12/13/2001

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Elected 8p. is norgestimate as in cl 8.
+ 3p. of Cl. 4 elected.

Please search for 1 Cl. 8, having improved dissolution and release rate properties, when progestin is norgestimate and excipient is lactose.

Please see attached sheet

Thank you

Mary Jane Ruhl
Tech. Info. Specialist, STIC
TC-1600
CM-1, Room 6A-06
Phone: 605-1155

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher:	NA Sequence (#)		STN	
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up: 3/6/03	Bibliographic		Dr.Link	
Date Completed: 3/7/03	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time:	Other		Other (specify)	

PTO-1590 (8-01)

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=> d his

     FILE 'REGISTRY' ENTERED AT 13:42:01 ON 07 MAR 2003
L1             1 S NORGESTIMATE/CN
L2             1 S 35189-28-7/RN
               E LACTOSE/CN
L3             1 S E3
L4             1 S 63-42-3/RN

     FILE 'HCAPLUS' ENTERED AT 13:43:25 ON 07 MAR 2003
L5          6084 S L2 OR ?NORGESTIMAT? OR ?PROGESTIN?
L6        137659 S L4 OR ?LACTOS? OR ?EXCIPIENT?
L7            42 S L5 AND L6
L8            21 S L7 AND ?CONTRACEPT?
L9             5 S L7 AND ?HORMON?(W)?REPLAC?(W)?THERAP?
L10            2 S L7 AND (?SOLUBIL? OR ?SOLUT?)
L11            1 S L7 AND (NON(W)?CRYSTAL? OR ?NONCRYSTAL?)
L12           23 S L8 OR L9 OR L10 OR L11

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     13:52:09 ON 07 MAR 2003
L13           33 S L12
L14           27 DUP REMOV L13 (6 DUPLICATES REMOVED)

     FILE 'HCAPLUS' ENTERED AT 14:36:55 ON 07 MAR 2003
L15          220 S L2 OR ?NORGESTIMATE?
L16        52091 S L4 OR LACTOSE OR ?EXCIPIENT?
L17            8 S L15 AND L16

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     14:39:15 ON 07 MAR 2003
L18            1 S L17
```

Truncation here yielded galactose - resulted in "false drops"

(1) Broader Search

(2) Narrow Search - avoided "false drops"

Can print these if you want to go even broader!

[redacted] Search


```
=> d que stat l12
L2            1 SEA FILE=REGISTRY ABB=ON  35189-28-7/RN
L4            1 SEA FILE=REGISTRY ABB=ON  63-42-3/RN
L5         6084 SEA FILE=HCAPLUS ABB=ON  L2 OR ?NORGESTIMAT? OR ?PROGESTIN?
L6       137659 SEA FILE=HCAPLUS ABB=ON  L4 OR ?LACTOS? OR ?EXCIPIENT?
L7           42 SEA FILE=HCAPLUS ABB=ON  L5 AND L6
L8           21 SEA FILE=HCAPLUS ABB=ON  L7 AND ?CONTRACEPT?
L9            5 SEA FILE=HCAPLUS ABB=ON  L7 AND ?HORMON?(W)?REPLAC?(W)?THERAP?

L10           2 SEA FILE=HCAPLUS ABB=ON  L7 AND (?SOLUBIL? OR ?DISOLUT?)
L11           1 SEA FILE=HCAPLUS ABB=ON  L7 AND (NON(W)?CRYSTAL? OR ?NONCRYSTAL
                ?)
L12          23 SEA FILE=HCAPLUS ABB=ON  L8 OR L9 OR L10 OR L11

=> d ibib abs hitrn 1-23 l12

L12  ANSWER 1 OF 23  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2002:465824  HCAPLUS
DOCUMENT NUMBER:          137:37670
TITLE:                    Steroid hormone products containing excipients
                          with improved dissolution properties
INVENTOR(S):              Schultz, Thomas; Clark, Bradley A.; Falzone, Angela
PATENT ASSIGNEE(S):       Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE:                   PCT Int. Appl., 26 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
     WO 2002047693      A2   20020620      WO 2001-US48862   20011213
     WO 2002047693      A3   20021107
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2002027421      A5   20020624      AU 2002-27421     20011213
     US 2002173669      A1   20021121      US 2001-22138     20011213
PRIORITY APPLN. INFO.:                  US 2000-255669P  P  20001214
                                        WO 2001-US48862  W  20011213
AB   The present invention relates to steroid hormone products, such as oral
     contraceptive products, including at least one steroid active
     ingredient mixed with an excipient and having improved dissoln.
     and release rate properties. The invention further relates to methods for
     making such steroid hormone products, wherein a mixt. of the hormone and
     the excipient is subjected to sufficient mech. energy to form a
     powder blend wherein the hormone is stabilized by the excipient
     in substantially non-cryst. form. An amorphous
     lactose-norgestimate dry ground mixt. was prepd.
IT   63-42-3, Lactose
     RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical
     process); PRP (Properties); PYP (Physical process); THU (Therapeutic use);
     BIOL (Biological study); PROC (Process); USES (Uses)
```

(steroid hormone products contg. **excipients** with improved dissoln. properties)

IT **35189-28-7, Norgestimate**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(steroid hormone products contg. **excipients** with improved dissoln. properties)

L12 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220377 HCAPLUS
DOCUMENT NUMBER: 136:252498
TITLE: Novel topical oestroprogestational compositions with systemic effect
INVENTOR(S): Gray, Georges; Villet, Bertrand; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex Sam, Monaco
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022132	A2	20020321	WO 2001-FR2865	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2814074	A1	20020322	FR 2000-11791	20000915
AU 2001090026	A5	20020326	AU 2001-90026	20010914
BR 2001007216	A	20020709	BR 2001-7216	20010914
EP 1265617	A2	20021218	EP 2001-969895	20010914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002002292	A	20020715	NO 2002-2292	20020514

PRIORITY APPLN. INFO.: FR 2000-11791 A 20000915
WO 2001-FR2865 W 20010914

AB The invention concerns the field of therapeutic chem. and more particularly the prodn. of novel galenic forms to be applied on the skin. More particularly, it concerns a topical hormonal compn. with systemic effect for hormonal treatment of perimenopause and menopause as well as for treating ovarian hormonal deficiency in a woman suffering from amenorrhea. The invention is characterized in that it comprises, as active principles, a progestational deriv. of the 19-norprogesterone and estradiol or one of its derivs., a carrier for systemic delivery of said active principles, selected among the group consisting of a film-forming agent, a gelling agent and mixts. thereof, combined with a mixt. of **excipients** suited for producing a gelled and/or film-forming pharmaceutical form. A topical gel contained nomegestrol acetate 0.4, estradiol 0.1, Carbopol-1342 0.5, propylene glycol 6, transcutol 5, EDTA 0.05, triethanolamine 0.3, water 42.65, and ethanol 45%. Effectiveness of the compn. was tested in female volunteers.

L12 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:667761 HCAPLUS
DOCUMENT NUMBER: 135:366893
TITLE: Assessment of the oestrogenic activity of the **contraceptive progestin** levonorgestrel and its non-phenolic metabolites
AUTHOR(S): Santillan, R.; Perez-Palacios, G.; Reyes, M.; Damian-Matsumura, P.; Garcia, G. A.; Grillasca, I.; Lemus, A. E.
CORPORATE SOURCE: Department of Reproductive Biology, National Institute of Medical Sciences and Nutrition S. Zubiran, Mexico City, Mex.
SOURCE: European Journal of Pharmacology (2001), 427(2), 167-174
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Levonorgestrel, a potent **contraceptive progestin** stimulates growth and proliferation of cultured breast cancer cells through a receptor-mediated mechanism, even though levonorgestrel does not bind to the estrogen receptor (ER). To assess whether the estrogen-like effects induced by this synthetic **progestin** are exerted via its metabolic conversion products, we studied the binding affinity of three A-ring levonorgestrel derivs. to the ER and their capability to transactivate an estrogen-dependent yeast system co-transfected with the human ER gene and estrogen responsive elements fused to a .beta.-**galactosidase** reporter vector. The results demonstrated that the 3.beta.,5.alpha. reduced levonorgestrel deriv. and to a lesser extent its 3.alpha. isomer interact with the estrogen receptor, with a significantly lower relative binding affinity (2.4% and 0.4%, resp.) than that of estradiol (100%), while levonorgestrel does not. Both levonorgestrel metabolites were able to activate, in a dose-dependent manner, the .beta.-**galactosidase** reporter gene in the yeast expression system, an effect that was precluded by a steroidal antiestrogen. The estrogenic potency of levonorgestrel metabolites was significantly lower (750-fold) than that of estradiol. Furthermore, high doses of 3.beta.,5.alpha. levonorgestrel (2.5 mg/day/6 days) induced an increase of estrogen-dependent **progestin** receptor in the anterior pituitary of castrated rats. The overall data offer a plausible explanation for the weak estrogenic effects induced by high, non-pharmacol. doses of levonorgestrel.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:629790 HCAPLUS
DOCUMENT NUMBER: 133:183039
TITLE: Novel **contraceptive** compositions and preparation process thereof
INVENTOR(S): He, Changhai; Ye, Zhihou; Gui, Youlun; Chen, Hailin
PATENT ASSIGNEE(S): Shanghai Birth Control Science Inst., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CN 1231177	A	19991013	CN 1998-106375	19980408
PRIORITY APPLN. INFO.:			CN 1998-106375	19980408

AB The **contraceptive** compn. [capsule] is composed of **progestin** antagonist, 0.05-0.25% surfactant, and **excipients**. The ratio of surfactant to **progestin** antagonist is 0.01- 0.5. The **progestin** antagonist is selected from mifepristone, lilopristone, and onapristone; and the surfactant from K-12, Na hexadecylsulfonate, Na octadecylsulfonate, Span-20, Span-60, Tween-80, Tween-60, polyoxyethylene monostearate, polyoxyethylene hexadecyl ether, and polyoxyethylene nonylphenyl ether. The **contraceptive** compn. is prepd. by milling or recrystg. **progestin** antagonist with solvent to obtain 5- 30 .PHI.mm particle, and mixing with surfactant and medicinal adjuvant. The content of mifepristone was detd. by HPLC at 302 nm on ODS column with methanol-acetonitrile-water (42:28:30, vol./vol.) (pH 4.7) as mobile phase.

L12 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	2000:439950 HCAPLUS
DOCUMENT NUMBER:	133:145020
TITLE:	The estrogenic effects of gestodene, a potent **contraceptive progestin**, are mediated by its A-ring reduced metabolites
AUTHOR(S):	Lemus, A. E.; Zaga, V.; Santillan, R.; Garcia, G. A.; Grillasca, I.; Damian-Matsumura, P.; Jackson, K. J.; Cooney, A. J.; Larrea, F.; Perez-Palacios, G.
CORPORATE SOURCE:	Department of Reproductive Biology, Universidad Autonoma Metropolitana-Iztapalapa, Mexico City, Mex.
SOURCE:	Journal of Endocrinology (2000), 165(3), 693-702 CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER:	Society for Endocrinology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Gestodene (17.alpha.-ethynyl-13.beta.-ethyl-17.beta.-hydroxy-4,15-gonadien-3-one) is the most potent synthetic **progestin** currently available and it is widely used as a fertility regulating agent in a no. of **contraceptive** formulations because of its high effectiveness, safety and acceptability. The observation that **contraceptive** synthetic **progestins** exert hormone-like effects other than their progestational activities, prompted the authors to investigate whether gestodene (GSD) administration may induce estrogenic effects, even though the GSD mol. does not interact with intracellular estrogen receptors (ER). To assess whether GSD may exert estrogenic effects through some of its neutral metabolites, a series of exptl. studies were undertaken using GSD and three of its A-ring reduced metabolites. Receptor binding studies by displacement anal. confirmed that indeed GSD does not bind to the ER, whereas its 3.beta.,5.alpha.-tetrahydro reduced deriv. (3.beta.GSD) interacts with a relative high affinity with the ER. The 3.alpha.,5.alpha. GSD isomer (3.alpha.GSD) also binds to the ER, though to a lesser extent. The ability of the A-ring reduced GSD derivs. to induce estrogenic actions was evaluated by the use of two different mol. bioassays: (a) transactivation of a yeast system cotransfected with the human ER.alpha. (hER.alpha.) gene and estrogen responsive elements fused to the .beta.-**galactosidase** reporter vector and (b) transactivation of the hER.alpha.-mediated transcription of the chloramphenicol acetyltransferase (CAT) reporter gene in a HeLa cells expression system. The estrogenic potency of 3.beta.GSD was also assessed by its capability to induce estrogen-dependent **progestin** receptors (PR) in the anterior pituitary of castrated female rats. The

results demonstrated that 3.beta.GSD and 3.alpha.GSD were able to activate, in a dose-dependent manner, the hER.alpha.-mediated transcription of both the .beta.-**galactosidase** and the CAT reporter genes in the yeast and HeLa cells expression systems resp. In both assays the 3.beta. deriv. of GSD exhibited a significantly greater estrogenic effect than its 3.alpha. isomer, while unchanged GSD and 5.alpha.GSD were completely ineffective. Neither 3.beta.GSD nor 3.alpha.GSD exhibited estrogen synergistic actions. Interestingly, the pure steroidal anti-estrogen ICI-182,780 diminished the transactivation induced by 3.beta.GSD and 3.alpha.GSD in the yeast expression system. Furthermore, administration of 3.beta.GSD resulted in a significant increase of estrogen-dependent PR in the anterior pituitaries of castrated rats in comparison with vehicle-treated animals. The characteristics of the 3.beta.GSD-induced PR were identical to those induced by estradiol benzoate. The overall results demonstrate that 3.beta.GSD and its 3.alpha. isomeric alc. specifically bind to the ER and possess a weak intrinsic estrogenic activity, whereas unmodified GSD does not. The data contribute to a better understanding of the GSD mechanism of action and allow the hypothesis to be advanced that the slight estrogen-like effects attributable to GSD are mediated by its non-phenolic, tetrahydro reduced metabolites.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:690944 HCAPLUS
DOCUMENT NUMBER: 131:303398
TITLE: Folic acid-containing pharmaceutical compositions comprising either an oral **contraceptive** or a hormone replacement composition
INVENTOR(S): Kafrissen, Michael E.
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA; United States Dept. of Health and Human Services
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953910	A2	19991028	WO 1999-US8429	19990416
WO 9953910	A3	19991229		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2329005	AA	19991028	CA 1999-2329005	19990416
AU 9935676	A1	19991108	AU 1999-35676	19990416
EP 1071428	A2	20010131	EP 1999-917591	19990416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6190693	B1	20010220	US 1999-292027	19990416
JP 2002512185	T2	20020423	JP 2000-544315	19990416

PRIORITY APPLN. INFO.: US 1998-82068P P 19980417

WO 1999-US8429 W 19990416

AB Folic acid-contg. pharmaceutical compns. comprising either an oral **contraceptive** or a hormone replacement compn. are disclosed. This invention also provides methods of administering folic acid to a subject using the instant pharmaceutical compns. Finally, this invention provides a drug delivery system useful for administering the instant pharmaceutical compns. An oral **contraceptive** contained ethinyl estradiol 35, folic acid 400 .mu.g, norethindrone 1.0 mg, **lactose**, pregelatinized starch and magnesium stearate q.s.

IT **35189-28-7, Norgestimate**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(folic acid-contg. pharmaceutical compns. comprising either oral **contraceptive** or hormone replacement compn.)

L12 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:45001 HCAPLUS
DOCUMENT NUMBER: 130:100684
TITLE: Oral **contraceptive** comprising **progestin**/estrogen combination
INVENTOR(S): Gast, Michael J.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5858405	A	19990112	US 1997-887162	19970702
ZA 9800539	A	19990722	ZA 1998-539	19980122

PRIORITY APPLN. INFO.: US 1997-887162 A 19970702

AB A bridged triphasic combination **progestin**/estrogen oral **contraceptive** regimen is provided comprising the administration of a **contraceptive progestin**/estrogen combination for 23-25 days consecutive days beginning on the first day of menses, followed by the administration of an estrogen for 3-5 days following the administration of the estrogen/**progestin** combination, so that the total period of administration is 28 days per 28 day cycle. Particularly preferred **progestins** of this invention are trimegestone, dienogest, and drospirenone. A tablet contained trimegestone 125, ethinyl estradiol 15, microcryst. cellulose, **lactose**, polaciillin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and water q.s. for a tablet.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:498263 HCAPLUS
DOCUMENT NUMBER: 129:140685
TITLE: Oral **contraceptive** preparation for men
INVENTOR(S): Oettel, Michael; Huebler, Doris; Schroeder, Jens; Dittgen, Michael
PATENT ASSIGNEE(S): Jenapharm G.m.b.H. und Co. K.-G., Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19650352	A1	19980730	DE 1996-19650352	19961204

PRIORITY APPLN. INFO.: DE 1996-19650352 19961204

AB An oral **contraceptive** for men contains DHEA or a natural or synthetic DHEA deriv. combined with a gestagen. The redn. in serum testosterone level induced by administration of gestagen alone, which causes a redn. in libido, is reversed by DHEA. Thus, a mixt. of DHEA 150.000, desogestrel 0.500, **lactose** 27.850, potato starch 15.000, PVP 1.500, Mg stearate 0.500, talc 1.500, and water 1.500 mg was granulated and formed into tablets which were coated with a mixt. of sucrose 19.60875, glucose syrup 1.37500, CaCO3 2.00000, Polyvidone K 25 0.12500, Macrogol 1.12500, TiO2 0.54546, yellow Fe oxide 0.06818, red Fe oxide 0.06818, brown Fe oxide 0.06818, and carnauba wax 0.01625 mg.

IT **35189-28-7, Norgestimate**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **contraceptive** prepn. for men)

L12 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:98330 HCAPLUS
DOCUMENT NUMBER: 128:158938
TITLE: Monophasic **contraceptive** method and kit comprising a combination of a **progestin** and estrogen
INVENTOR(S): Gast, Michael Jay
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804269	A1	19980205	WO 1997-US12795	19970723
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2261689	AA	19980205	CA 1997-2261689	19970723
AU 9738887	A1	19980220	AU 1997-38887	19970723
AU 726091	B2	20001102		
BR 9710566	A	19990817	BR 1997-10566	19970723
CN 1226168	A	19990818	CN 1997-196763	19970723
EP 956024	A1	19991117	EP 1997-936149	19970723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2000515890	T2	20001128	JP 1998-508924	19970723
KR 2000029515	A	20000525	KR 1999-700553	19990123

PRIORITY APPLN. INFO.: US 1996-686790 A 19960726
WO 1997-US12795 W 19970723

AB A method of **contraception** is provided which comprises administering to a female of child bearing age a combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 23-25 days beginning on day 1 of the menstrual cycle, and wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 23-25 days. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, **lactose**, potassium polacrillin,magnesium stearate, Opadry pink, PEG-1500, was E, and water q.s.

L12 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:98329 HCAPLUS
DOCUMENT NUMBER: 128:158937
TITLE: **Progestin**/estrogen oral **contraceptives**
INVENTOR(S): Gast, Michael Jay
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804268	A1	19980205	WO 1997-US12786	19970723
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2261687	AA	19980205	CA 1997-2261687	19970723
AU 9738076	A1	19980220	AU 1997-38076	19970723
AU 713016	B2	19991118		
EP 917466	A1	19990526	EP 1997-935047	19970723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9710565	A	19990817	BR 1997-10565	19970723
CN 1230888	A	19991006	CN 1997-198093	19970723
JP 2000515888	T2	20001128	JP 1998-508919	19970723
KR 2000029537	A	20000525	KR 1999-700594	19990125

PRIORITY APPLN. INFO.: US 1996-686786 A 19960726
WO 1997-US12786 W 19970723

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days, a first phase combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 3-8 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 3-8 days. A

second phase combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days, beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 4-15 days, and a third phase combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 4-15 days provided that the daily dosage of the combination administered in the phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, **lactose**, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

L12 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:98327 HCAPLUS
DOCUMENT NUMBER: 128:158935
TITLE: **Progestin**/estrogen oral **contraceptives**
INVENTOR(S): Gast, Michael Jay
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804266	A1	19980205	WO 1997-US12788	19970723
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9739616	A1	19980220	AU 1997-39616	19970723
PRIORITY APPLN. INFO.:			US 1996-688177	19960726
			WO 1997-US12788	19970723

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 28 consecutive days, a first phase combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, and 250 .mu.g-4 mg drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 9-13 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 9-13 days. A second phase combination of a **progestin** at a daily dosage of

40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, and 250 .mu.g-4 mg drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 11-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 11-15 days, and an estrogen phase estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 3-5 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the estrogen is administered in each of the 3-5 days, provided that the daily dosage of second phase **progestin** is greater than the daily dosage of the first phase **progestin** and that the daily dosage of the second phase estrogen. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, **lactose**, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

L12 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:98326 HCAPLUS
DOCUMENT NUMBER: 128:158934
TITLE: Biphasic **contraceptive** method and kit comprising a combination of a **progestin** and estrogen
INVENTOR(S): Gast, Michael Jay
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804265	A1	19980205	WO 1997-US12787	19970723
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2261748	AA	19980205	CA 1997-2261748	19970723
AU 9740435	A1	19980220	AU 1997-40435	19970723
EP 921804	A1	19990616	EP 1997-938011	19970723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
CN 1226167	A	19990818	CN 1997-196684	19970723
JP 2000515889	T2	20001128	JP 1998-508920	19970723
PRIORITY APPLN. INFO.:			US 1996-690422 A	19960726
			WO 1997-US12787 W	19970723

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days, a first phase combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 9-13 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 9-13 days, and a

second phase combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 11-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 11-15 days, provided that the daily dosage of second phase **progestin** is greater than the daily dosage of the first phase **progestin** and that the daily dosage of the second phase estrogen is greater than or equal to the daily dosage of the first phase estrogen. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 10 .mu.g, microcryst. cellulose, **lactose**, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

L12 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:98311 HCAPLUS
DOCUMENT NUMBER: 128:158929
TITLE: Oral **contraceptives** containing combination of a **progestin** and an estrogen
INVENTOR(S): Gast, Michael Jay
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804246	A2	19980205	WO 1997-US12785	19970723
WO 9804246	A3	20020926		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9738885	A1	19980220	AU 1997-38885	19970723

PRIORITY APPLN. INFO.: US 1996-690439 A 19960726
WO 1997-US12785 W 19970723

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days: a first phase combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 3-8 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 3-8 days; a second phase combination of a **progestin** at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 4-15 days. A third phase combination of a **progestin** at a daily dosage of 40-500

.mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g drospirenone, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the **progestin** and estrogen combination is administered in each of the 4-15 days; and an estrogen phase estrogen at a daily dosage equiv. in estrogenic activity to 5-20 .mu.g ethinyl estradiol, for 3-5 days beginning on the day immediately following the last day of administration of the third phase combination, wherein the same dosage of the estrogen is administered in each of the 3-5 days, provided that the daily dosage of the combination administered in the first phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcrystaline cellulose, **lactose**, potassium polacrillin, magnesium stearate, Opadry pink, PEG-1500, was E, and water q.s.

L12 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:42284 HCAPLUS
DOCUMENT NUMBER: 128:119658
TITLE: Progestogen-anti-progestogen regimen and formulations
INVENTOR(S): Coelingh Bennink, Herman Jan Tijmen; Verbost, Pieter M.
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.; Coelingh Bennink, Herman Jan Tijmen; Verbost, Pieter M.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9749407	A1	19971231	WO 1997-EP3288	19970623
W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, TR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9734360	A1	19980114	AU 1997-34360	19970623
AU 725670	B2	20001019		
EP 912186	A1	19990506	EP 1997-930384	19970623
EP 912186	B1	20020306		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1223585	A	19990721	CN 1997-195800	19970623
BR 9709934	A	19990810	BR 1997-9934	19970623
JP 2000514785	T2	20001107	JP 1998-502338	19970623
AT 213947	E	20020315	AT 1997-930384	19970623
RU 2189819	C2	20020927	RU 1999-101114	19970623
ES 2174265	T3	20021101	ES 1997-930384	19970623
NO 9806104	A	19981223	NO 1998-6104	19981223
KR 2000022189	A	20000425	KR 1998-710607	19981224
US 2001027189	A1	20011004	US 2001-757048	20010108
US 6506390	B2	20030114		

PRIORITY APPLN. INFO.:
EP 1996-201744 A 19960625
WO 1997-EP3288 W 19970623
US 1998-194134 B1 19981120

AB A **contraceptive** and/or HRT (**hormone**

replacement therapy) kit comprises sequential daily dosage units each contg. a progestogen, or as effective ingredient for HRT a progestogen with or without an estrogen or an estrogen only, and 2 or more dosage units comprising an anti-progestogen. One of the anti-progestogen is administered at the beginning and the others regularly divided throughout the cycle, preferably one only in the middle of the cycle. Thus, tablets contained desogestrel 0.075, corn starch 6.500, Povidone 1.950, stearic acid 0.650, colloidal siO2 0.650, dl-.alpha.-tocopherol 0.080, and **lactose** qs 65.000 mg/tablet. The coating layer contained HPMC 0.75, PEG-400 0.15, TiO2 0.1125, and talc 0.1875 mg/tablet.

L12 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:692817 HCAPLUS
DOCUMENT NUMBER: 126:42800
TITLE: Increased levels of several lysosomal enzymes in sera from women using oral **contraceptives**
AUTHOR(S): Sanchez-Martin, M. Mario; Cabezas-Delamare, Manuel J.; Cabezas, Jose A.
CORPORATE SOURCE: Departamento de Bioquimica y Biologia Molecular, Facultad de Biologia, Avenida del Campo Charro s/n, E-37007-Salamanca, Spain
SOURCE: Clinica Chimica Acta (1996), 255(2), 173-181
CODEN: CCATAR; ISSN: 0009-8981
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The activities of eight lysosomal enzymes were measured by spectrophotometric/spectrofluorimetric techniques in the blood sera of 19-24 apparently healthy women using an oral **contraceptive** (**progestin** and estradiol synthetic deriv., desogestrel+ethinylestradiol) in comparison with 15-16 non-pregnant women not using **contraceptives** (controls), in a randomized, double-blind, controlled study. .beta.-Glucuronidase and arylesterase showed statistically increased activities in the exptl. group in comparison to the controls. No significant differences were found for the remaining enzymes assayed (.beta.-N-acetylhexosaminidase, .alpha.-L-fucosidase, .alpha.-mannosidase, .beta.-**galactosidase**, .alpha.-**galactosidase** and acid phosphatase). Similar results were obtained when the **contraceptive** formed by the combination of levonorgestrel and ethinylestradiol was used by an exptl. group of eight healthy women. These results suggest that the significant increases in the above-mentioned activities might be the physiol. response of the organism (through catabolic processes catalyzed by lysosomal enzymes) to the administration of exogenous synthetic compds., such as the oral **contraceptives** used.

L12 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:194879 HCAPLUS
DOCUMENT NUMBER: 124:242335
TITLE: Pharmaceutical preparation for **contraception** and hormone substitution with biogenic estrogen components
INVENTOR(S): Oettel, Michael; Osterwald, Hermann; Moore, Claudia; Graeser, Thomas
PATENT ASSIGNEE(S): Jenapharm GmbH, Germany
SOURCE: Ger., 8 pp.
CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4429374	C1	19960201	DE 1994-4429374	19940812
EP 696454	A2	19960214	EP 1995-250153	19950628
EP 696454	A3	19960717		
EP 696454	B1	19990929		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 185072	E	19991015	AT 1995-250153	19950628
US 5633242	A	19970527	US 1995-511026	19950803
JP 08169833	A2	19960702	JP 1995-205801	19950811
JP 3002117	B2	20000124		

PRIORITY APPLN. INFO.: DE 1994-4429374 A 19940812

AB A 3-stage hormone treatment regimen effective for either **contraception** or **hormone replacement therapy** in women comprises (1) 3 or 4 daily dosage units of biogenic estrogen (e.g. 17.beta.-estradiol), (2) 20-22 daily dosage units of biogenic estrogen/C21 gestagen combination, and (3) 3 or 4 daily dosage units of biogenic estrogen. Continuation of estrogen administration throughout the 28-day treatment cycle avoids the bleeding and other side effects of interruption of estrogen administration seen in the prior art, and provides excellent control of the ovarian cycle. Thus, suitable compns. of tablets for the 3 treatment stages (1 tablet/day) were: (stage 1) micronized estradiol valerate 2.0, **lactose** 33.4, corn starch 17.2, PVP 2.1, and Mg stearate 0.3 mg (4 tablets); (stage 2) micronized estradiol 2.0, micronized dienogest 2.0, **lactose** 33.4, corn starch 17.2, PVP 2.1, and Mg stearate 0.3 mg (7 tablets), followed by micronized estradiol 4.0, micronized dienogest 2.0, **lactose** 33.4, corn starch 17.2, PVP 2.1, and Mg stearate 0.3 mg (14 tablets); (stage 3) micronized estradiol valerate 2.0, **lactose** 33.4, corn starch 17.2, PVP 2.1, and Mg stearate 0.3 mg (3 tablets).

IT **35189-28-7, Norgestimate**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical prepn. for **contraception** and hormone substitution with biogenic estrogen components)

L12 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:418053 HCAPLUS
DOCUMENT NUMBER: 121:18053
TITLE: Readily resorbable gestagen-containing pharmaceutical composition
INVENTOR(S): Oettel, Michael; Osterwald, Hermann; Dittgen, Michael
PATENT ASSIGNEE(S): Jenapharm GmbH, Germany
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 587047	A2	19940316	EP 1993-114056	19930902
EP 587047	A3	19970115		
EP 587047	B1	20011212		
R: DE, DK, ES, FR, GB, IT, SE				

DE 4229820	A1	19940317	DE 1992-4229820	19920907
DE 4229820	C2	19981203		
ES 2169722	T3	20020716	ES 1993-114056	19930902

PRIORITY APPLN. INFO.: DE 1992-4229820 A 19920907

AB Gestagens embedded in gel-forming carboxyvinyl polymers and placed in close contact with the skin or mucosa are resorbed rapidly and practically quant. for **hormone replacement therapy**, e.g. treatment of climacteric and postmenopausal problems and osteoporosis. Thus, a mixt. of micronized desogestrel, **lactose**, potato starch, and Na carboxymethylstarch was spray-coated with Eudragit E30D, granulated, mixed with Mg stearate, and packed into hard gelatin capsules. On disintegration of the capsule in the intestine, the contents form a gel which adheres to the intestinal mucosa, allowing diffusion of desogestrel into the mucosa.

IT **35189-28-7, Norgestimate**
RL: BIOL (Biological study)
(carboxyvinyl polymer-embedded, resorption of, by mucosa and skin)

L12 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:253387 HCAPLUS
DOCUMENT NUMBER: 120:253387
TITLE: Antiprogestogen-containing **contraceptives**
INVENTOR(S): Bergink, Engelbert Willem
PATENT ASSIGNEE(S): AKZO N. V., Neth.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9404156	A1	19940303	WO 1993-EP2139	19930810
W: AU, CA, FI, JP, KR, NO, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9305617	A	19940307	ZA 1993-5617	19930803
AU 9347089	A1	19940315	AU 1993-47089	19930810

PRIORITY APPLN. INFO.: EP 1992-202504 A 19920814
WO 1993-EP2139 W 19930810

AB An effective oral **contraceptive** compn. is comprised of an antiprogestogen phase combined with a progestogenic phase. The **contraceptive** compn. has a first phase of 5-20, esp. 14, sequential daily dosage units contg. an antiprogestogen at a daily dosage sufficient to inhibit ovulation in the female, and a second phase of 10 to 25, esp. 14, sequential daily dosage units contg. a progestogen at a dosage equiv. to 40-120 .mu.g desogestrel administered orally. To the first phase is preferentially added an estrogen such as 17.beta.-estradiol (I) (0.50-2.5 mg daily) to allow for the possibility of making a sequential regimen. A **contraceptive** tablets contained in the first phase (14 tablets) (6.beta.,11.beta., 17.beta.)-11-(4-dimethylaminophenyl)-6-methyl-4',5,-dihydorspiro[estra-4,9-diene-17,2'(3'H)-furan]-3-one 20.00, I 1.00, corn starch 8.00, PVP 2.40, stearic 0.80, silica 0.08, dL-.alpha.-tocopherol 0.08, and **lactose** q.s. 80.00mg; and in the second phase (14 tablets) desogestrel 0.075, corn starch 8.000, PVP 2.400, stearic acid 0.0800, silica 0.0800, dL-.alpha.-tocopherol 0.0800, and **lactose** q.s. 80.000mg.

IT **35189-28-7, Norgestimate**
RL: BIOL (Biological study)
(female **contraceptives** contg. antiprogestogens and)

L12 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:39773 HCAPLUS
DOCUMENT NUMBER: 104:39773
TITLE: Triphasic oral **contraceptive**
INVENTOR(S): Pasquale, Samuel A.
PATENT ASSIGNEE(S): Ortho Pharmaceutical Corp., USA
SOURCE: U.S., 5 pp. Cont.-in-part of U.S. Ser. No. 536,135.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

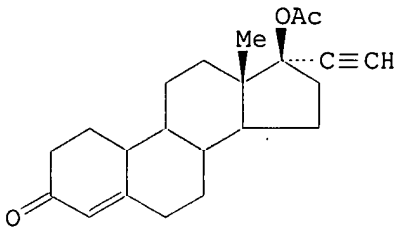
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4544554	A	19851001	US 1984-607038	19840504
US 4530839	A	19850723	US 1983-536135	19830926
CA 1226221	A1	19870901	CA 1984-462334	19840904
US 4628051	A	19861209	US 1985-743344	19850611
US 4616006	A	19861007	US 1985-744189	19850613

PRIORITY APPLN. INFO.: US 1983-536135 19830926
US 1984-607038 19840504

AB The title **contraceptive** compn. comprises 21 sep. daily dosage units adapted for successive daily oral ingestion, wherein the estrogen dosage is kept const. throughout the 21-day cycle, whereas the progestogen dosage is gradually increased in successive doses. The combination consists as the 1st, 2nd, and 3rd phases, 5-8, 7-11, and 3-7 dosage units, resp., of an estrogen and progestogen. Then, for 6-8 days either estrogen or progestogen was not administered. Thus, a 1st stage tablet contained 17-.alpha.-ethinylestradiol 0.035, norethindrone 0.50, **lactose** 88.9, pregelatinized starch 10.0, and Mg stearate 0.5 mg. The 2nd and 3rd stage tablets contained the same amt. of each ingredient, except for norethindrone which was 0.75 and 1.0 mg, resp.

IT **35189-28-7**
RL: BIOL (Biological study)
(triphasic oral **contraceptives** contg. ethinylestradiol and)

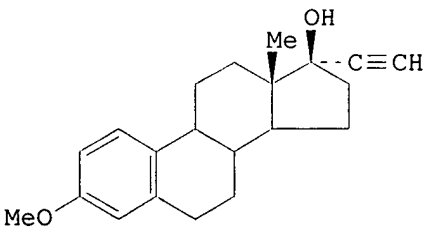
L12 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1979:529076 HCAPLUS
DOCUMENT NUMBER: 91:129076
TITLE: Application of sodium borohydride method for the determination of norethisterone acetate in **contraceptive** tablets
AUTHOR(S): Eldawy, Mohamed A.; Tawfik, A. S.; Elshabouri, S. R.
CORPORATE SOURCE: Fac. Pharm., Univ. Assiut, Assiut, Egypt
SOURCE: Egyptian Journal of Chemistry (1978), Volume Date 1976, 19(3), 461-5
CODEN: EGJCA3; ISSN: 0367-0422
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



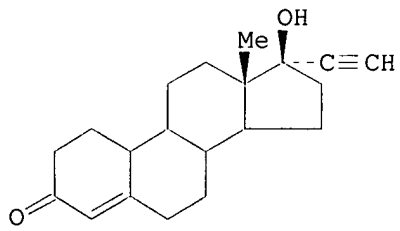
I

AB A differential UV spectrophotometric procedure was developed for the anal. of norethisterone acetate (I) [51-98-9] in **contraceptive** tablets. Common **excipients** and coating materials do not interfere with the proposed method. Ethinylestradiol, the estrogen commonly encountered along with the title **progestin** in **contraceptive** tablets does not interfere either. A std. deviation of 0.5% was obtained on com. available **contraceptives**.

L12 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:94887 HCAPLUS
DOCUMENT NUMBER: 88:94887
TITLE: Simultaneous gas-chromatographic determination of mestranol and norethisterone in oral estrogen-**progestin** combinations
AUTHOR(S): Moretti, G.; Cavina, G.; Chiappetta, G.; Fattori, I.; Petrella, M.; Pompi, V.
CORPORATE SOURCE: Lab. Biol., Ist. Super. Sanita, Rome, Italy
SOURCE: Bollettino Chimico Farmaceutico (1977), 116(8), 463-72
CODEN: BCFAAI; ISSN: 0006-6648
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI



I



II

AB Mestranol (I) [72-33-3] and norethisterone (II) [68-22-4] were detd. in estrogen-**progestin contraceptive** tablets contg. these 2 components by simple extn. with EtOAc and a single gas chromatog., with testosterone propionate as internal std. The recoveries of I and II were 98.54 and 99.14%, resp., and the precision (coeff. of variation) was 1.40 and 1.74%, resp. The procedure could be applied to single tablets contg. 0.05 mg I and 1 mg II. No interfering materials were extd. from the **excipient** by the EtOAc. Instrumental factors caused variations of <1%.

L12 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1975:536992 HCAPLUS
DOCUMENT NUMBER: 83:136992

TITLE: Rapid, sensitive colorimetric method for determination of ethinylestradiol
AUTHOR(S): Eldawy, Mohamed A.; Tawfik, A. S.; Elshabouri, S. R.
CORPORATE SOURCE: Fac. Pharm., Univ. Assiut, Assiut, Egypt
SOURCE: Journal of Pharmaceutical Sciences (1975), 64(7), 1221-3
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB A colorimetric procedure, based on the formation of an azo dye by condensation of diazotized 5-chloro-2,4-dinitroaniline with ethinylestradiol (I) [57-63-6] was developed. An alkaline soln. of I was reacted with the reagent, and the resulting color was measured at 450 nm. Absorbance versus concn. was linear .ltoreq.10 .mu.g/ml; the lower limit of detection was 1 .mu.g/ml under the conditions studied. Replicate anal. showed good agreement, and an av. recovery of 99.6 .+-. 0.3% was obtained for analyses of synthetic mixts. Vitamins and minerals likely to be present along with I in certain geriatric formulations, as well as ordinary tablet **excipients** and coating materials, do not interfere with the precision of the method or development of the color. The method was applicable to **progestin**-estrogen prepns. Assay results on various single-component as well as **contraceptive** com. samples were reported.
IT **63-42-3**
RL: ANST (Analytical study)
(ethinylestradiol detn. in presence of)

L12 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1969:520197 HCAPLUS
DOCUMENT NUMBER: 71:120197
TITLE: Minor hepatic reactions to the use of **contraceptive** estrogen-**progestin** preparations
AUTHOR(S): Toulet, J.; Hennequin, C.
CORPORATE SOURCE: Hop. Int., Paris, Fr.
SOURCE: Revue Internationale d'Hepatologie (1969), 19(3), 117-41
CODEN: RIHEAK; ISSN: 0556-7904
DOCUMENT TYPE: Journal
LANGUAGE: French
AB Prolonged use of estrogen-**progestin contraceptives** (2 months-4 years) by young women did not produce any significant changes in the amts. of bilirubin, alk. phosphatase, glutamic-oxalacetic and glutamic-pyruvate transaminase. Various liver tests showed slight anomalies in the water and **galactose** tests as well as in the bromsulfthalein test. These changes did not become more severe during prolonged use of the **contraceptive** compds.; however, they indicate frequent, although not obligatory, hepatic changes during prolonged use of these drugs.

```
=> d que stat l14
L2            1 SEA FILE=REGISTRY ABB=ON  35189-28-7/RN
L4            1 SEA FILE=REGISTRY ABB=ON  63-42-3/RN
L5         6084 SEA FILE=HCAPLUS ABB=ON  L2 OR ?NORGESTIMAT? OR ?PROGESTIN?
L6       137659 SEA FILE=HCAPLUS ABB=ON  L4 OR ?LACTOS? OR ?EXCIPIENT?
L7           42 SEA FILE=HCAPLUS ABB=ON  L5 AND L6
L8           21 SEA FILE=HCAPLUS ABB=ON  L7 AND ?CONTRACEPT?
L9            5 SEA FILE=HCAPLUS ABB=ON  L7 AND ?HORMON?(W)?REPLAC?(W)?THERAP?

L10           2 SEA FILE=HCAPLUS ABB=ON  L7 AND (?SOLUBIL? OR ?DISOLUT?)
L11           1 SEA FILE=HCAPLUS ABB=ON  L7 AND (NON(W)?CRYSTAL? OR ?NONCRYSTAL
                ?)
L12          23 SEA FILE=HCAPLUS ABB=ON  L8 OR L9 OR L10 OR L11
L13          33 SEA L12
L14          27 DUP REMOV L13 (6 DUPLICATES REMOVED)


=> d ibib abs l14 1-27

L14  ANSWER 1 OF 27  WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER:     2002-490577 [52]   WPIDS
DOC. NO. CPI:         C2002-139339
TITLE:                Steroid hormone product comprises a steroid hormone in
                      non crystalline form and a stabilizing
                      excipient, e.g. lactose, useful as an
                      oral contraceptive or HRT product.
DERWENT CLASS:        B01 B04
INVENTOR(S):          CLARK, B A; FALZONE, A; SCHULTZ, T
PATENT ASSIGNEE(S):   (ORTH) ORTHO-MCNEIL PHARM INC; (CLAR-I) CLARK B A;
                      (FALZ-I) FALZONE A; (SCHU-I) SCHULTZ T
COUNTRY COUNT:        98
PATENT INFORMATION:

     PATENT NO   KIND DATE     WEEK      LA   PG
     -------------------------------------------
     WO 2002047693 A2 20020620 (200252)* EN   26
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
            RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZM ZW
     AU 2002027421 A  20020624 (200267)
     US 2002173669 A1 20021121 (200279)

APPLICATION DETAILS:

     PATENT NO   KIND                  APPLICATION      DATE
     ------------------------------------------------------------
     WO 2002047693 A2                  WO 2001-US48862  20011213
     AU 2002027421 A                   AU 2002-27421    20011213
     US 2002173669 A1 Provisional      US 2000-255669P  20001214
                                       US 2001-22138    20011213

FILING DETAILS:

     PATENT NO   KIND                  PATENT NO
     ---------------------------------------------
     AU 2002027421 A  Based on         WO 200247693
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PRIORITY APPLN. INFO: US 2000-255669P 20001214; US 2001-22138 20011213
AN 2002-490577 [52] WPIDS
AB WO 200247693 A UPAB: 20020815
NOVELTY - A steroid hormone product comprises a steroid hormone in **non-crystalline** form and a stabilizing **excipient**, having improved dissolution and release rate properties.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preparing the steroid hormone product comprising preparing a mixture of at least one steroid hormone and at least one **excipient**, imparting mechanical energy to yield an **excipient**/hormone powder blend in **non-crystalline** form and forming the product from the powder blend.
ACTIVITY - **Contraceptive**.
No details of tests showing activity are given.
MECHANISM OF ACTION - None given.
USE - As oral **contraceptives** or **hormone replacement therapy** (HRT) products, (claimed).
ADVANTAGE - The product has improved dissolution and release rate.
Dwg.0/0

L14 ANSWER 2 OF 27 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-507991 [54] WPIDS
DOC. NO. CPI: C2002-144423
TITLE: New crystalline form of 6-hydroxy-3-(4-(2-(piperidin-1-yl)ethoxy)phenoxy)-2-(4-methoxyphenyl)benzo(b)thiophene hydrochloride for inhibiting pathological conditions e.g. uterine fibrosis.
DERWENT CLASS: B02
INVENTOR(S): LUKE, W D
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002034741	A2	20020502	(200254)*	EN	52

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002014534	A	20020506	(200257)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002034741	A2	WO 2001-US27773	20011018
AU 2002014534	A	AU 2002-14534	20011018

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002014534	A Based on	WO 200234741

PRIORITY APPLN. INFO: US 2000-242252P 20001020

AN 2002-507991 [54] WPIDS
AB WO 200234741 A UPAB: 20020823
NOVELTY - A crystalline form of 6-hydroxy-3-(4-(2-(piperidin-1-yl)ethoxy)phenoxy)-2-(4-methoxyphenyl)benzo(b)thiophene hydrochloride (A) confirmed by X-ray diffraction pattern is new. The diffraction pattern is obtained from a copper radiation source.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) Pharmaceutical formulation comprising (A), at least one carrier, diluent or **excipient**, and optionally a stabilizing agent (preferably methionine, (acetyl)cysteine or cysteine hydrochloride), and optionally an aromatase inhibitor, luteinizing hormone releasing hormone (LHRH) analog or preferably estrogen, **progestin** or an acetyl choline esterase (AChE) inhibitor, especially Premarin (RTM; estrogen-based compound);

(2) Up-regulation of choline acetyltransferase (ChAT) in mammals by administering (A) and optionally an AChE inhibitor; and

(3) Preparation of (A) from a crystallization solvent (preferably methanol or its aqueous form, ethanol or isopropanol, especially aqueous methanol (vol:vol) in a ratio of 20 - 5 (preferably 15)%) and subsequently drying the resulting solid to a constant weight.

ACTIVITY - Cytostatic; Gynecological; Vasotropic; Osteopathic; Cardiovascular-Gen.; Antilipemic; CNS-Gen.; Nootropic; Neuroprotective.

MECHANISM OF ACTION - Pathological condition inhibitor; ChAT up-regulator.

Test details are described but no results are given.

USE - In the manufacture of a medicament for inhibiting a pathological condition e.g. uterine fibrosis, endometriosis, aortal smooth muscle cell proliferation, restenosis, benign prostatic hyperplasia, bone loss, osteoporosis, cardiovascular disease, hyperlipidemia, central nervous system (CNS) disorders, Alzheimer's disease, cancer of the breast, uterus, ovaries, endometrium or prostate; and for up-regulating ChAT in mammals (claimed). Also for inhibiting diseases associated with estrogen deprivation.

ADVANTAGE - (A) is highly crystalline, non-solvated, anhydrous and can be reproducible and efficiently prepared on a commercial scale. (A) is more stable at ambient temperature and is therefore more amenable to pharmaceutical development. (A) does not show any propensity to adsorb water on changes in relative humidity. The crystal lattice of (A) is stable up to its melting temperature. (A) has 10% higher aqueous **solubility** as compared to its solvated forms and is the most stable known form.

Dwg.0/3

L14 ANSWER 3 OF 27 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-010408 [01] WPIDS
DOC. NO. CPI: C2002-002439
TITLE: Composition useful as oral **contraception** in cancer comprises a cyclic compound containing a ring system and a sulfamate group in a specified amount to provide a specified dosage.
DERWENT CLASS: B01
INVENTOR(S): ELGER, W; POTTER, V L B; PROSKE, H; REDDERSEN, G; REED, M J; POTTER, B V L; RODDERSEN, G
PATENT ASSIGNEE(S): (SCHD) SCHERING AG; (STER-N) STERIX LTD; (ELGE-I) ELGER W; (POTT-I) POTTER B V L; (PROS-I) PROSKE H; (REDD-I) REDDERSEN G; (REED-I) REED M J
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001051055	A2	20010719	(200201)*	EN	73
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001025331	A	20010724	(200201)		
US 2001021707	A1	20010913	(200201)		
ZA 2001000367	A	20020327	(200230)		71
NO 2002003392	A	20020916	(200273)		
EP 1248626	A2	20021016	(200276)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
BR 2001007630	A	20021008	(200277)		
CZ 2002002282	A3	20021113	(200282)		
SK 2002001002	A3	20021203	(200282)		
US 2002193444	A1	20021219	(200303)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2001051055	A2		WO 2001-GB94	20010111
AU 2001025331	A		AU 2001-25331	20010111
US 2001021707	A1	Provisional	US 2000-218730P	20000717
			US 2001-755429	20010105
ZA 2001000367	A		ZA 2001-367	20010112
NO 2002003392	A		WO 2001-GB94	20010111
			NO 2002-3392	20020712
EP 1248626	A2		EP 2001-900503	20010111
			WO 2001-GB94	20010111
BR 2001007630	A		BR 2001-7630	20010111
			WO 2001-GB94	20010111
CZ 2002002282	A3		WO 2001-GB94	20010111
			CZ 2002-2282	20010111
SK 2002001002	A3		WO 2001-GB94	20010111
			SK 2002-1002	20010111
US 2002193444	A1	Provisional	US 2000-218730P	20000717
		CIP of	US 2001-755429	20010105
			US 2002-120275	20020410

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001025331	A	Based on	WO 200151055
EP 1248626	A2	Based on	WO 200151055
BR 2001007630	A	Based on	WO 200151055
CZ 2002002282	A3	Based on	WO 200151055
SK 2002001002	A3	Based on	WO 200151055

PRIORITY APPLN. INFO: US 2000-218730P 20000717; GB 2000-792 20000114; GB 2000-2115 20000128

AN 2002-010408 [01] WPIDS

AB WO 200151055 A UPAB: 20020105

NOVELTY - A pharmaceutical composition comprises:

(i) a cyclic compound containing a ring system and a sulfamate group

in an amount to provide a dosage of no greater than 200 micro g/day; and

(ii) optionally mixing the compound with a carrier, diluent, **excipient** or adjuvant.

DETAILED DESCRIPTION - A pharmaceutical composition comprises:

(i) a compound of formula (I) in an amount, to provide a dosage of no greater than 200 micro g/day; and

(ii) optionally mixing (I) with a carrier, diluent, **excipient** or adjuvant.

X = hydrocarbyl ring having at least 4 atoms in the ring;

K' = hydrocarbyl group; and

Rs = sulfamate group.

ACTIVITY - Osteopathic; Cytostatic; Immunosuppressive; Gynecological; Nootropic; Neuroprotective; Antiinflammatory; Antiarthritic; Antirheumatic; Antidiabetic; Dermatological; Antithyroid; Antiulcer; Antipsoriatic; Antiasthmatic; Anticonvulsant.

MECHANISM OF ACTION - None given.

USE - In medicine, in the manufacture of a medicament for use in oral **contraception**, in **hormone replacement therapy**, for bone protecting **hormone replacement therapy** without endometrial stimulation; in the therapy of a condition or disease associated with steroid or steryl sulfatase (STS) or adverse STS levels (all claimed); in the treatment cancer e.g. breast cancer, ovarian cancer, endometrial cancer, sarcomas melanomas, prostate cancer, pancreatic cancer and other solid tumors, including hormone dependent and hormone independent cancers, as well as non-malignant conditions such as the prevention of auto-immune disease; in the therapeutic uses other than for the treatment of endocrine-dependent cancers; in the treatment of endometriosis and for therapy of estrogen-dependent tumors; in human or animal usage in human and veterinary medicine; in the treatment of neurodegenerative diseases; enhancing the memory function of patients suffering from illnesses such as amnesia, head injuries, Alzheimer's disease, epileptic dementia, pre-senile dementia, post traumatic dementia, senile dementia, vascular dementia and post-stroke dementia or individuals otherwise seeking memory enhancement; in TH1 implications; in treating inflammatory conditions such as autoimmunity e.g. rheumatoid arthritis, type I and II diabetes, systemic lupus erythematosus, multiple sclerosis, myasthenia gravis, thyroiditis, vasculitis, ulcerative colitis and Crohn's disease, skin disorders e.g. psoriasis and contact dermatitis; graft versus host disease; eczema, asthma and organ rejection following transplantation. The composition is also useful in the treatment of the disorders listed in WO-A-99/52890, WO-A-98/05635, WO-A-98/07859 and WO-A-98/09985.

ADVANTAGE - The dosage provided by the composition and the delivered compounds show a more favorable relation between desired and therapeutically undesired effects. The compounds have no or minimal, estrogenic effect. The composition provides improved pharmacokinetics and pharmacodynamics; provides a **hormone replacement therapy** for bone protection without endometrial stimulation; provides steady plasma levels of estrone and estradiol; can be formulated without the incorporation of **progestins** or gestagens. In a delivered dosage, the sulfamate compounds have a low hepatic metabolism and a high bioavailability, and EMATE has a high affinity to erythrocytes. The sulfamate compounds exhibit low variation in concentration in plasma between individuals. The reduction of estrogen levels in the blood allows provision of a mono product for both hysterectomized and non-hysterectomized subjects without the need to develop separate products. At the delivered dosage, the sulfamate compounds have a low hormone action and thus the risks of deep vein thrombosis are reduced. The compounds cause inhibition of growth of positive estrogen receptor positive (ER+) and ER negative (ER-) breast cancer cells in vitro by

preventing, inhibiting, arresting cell cycling; and/or causes regression of nitroso-methyl urea (NMU)-induced mammary tumors in intact animals (i.e. not ovariectomized), prevents, inhibits and/or arrests cell cycling in cancer cells; act in vivo by preventing, inhibiting, arresting cell cycling and/or act as a cell cycling agonist.
Dwg.0/11

L14 ANSWER 4 OF 27 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001510069 MEDLINE
DOCUMENT NUMBER: 21441621 PubMed ID: 11557270
TITLE: Assessment of the oestrogenic activity of the **contraceptive progestin** levonorgestrel and its non-phenolic metabolites.
AUTHOR: Santillan R; Perez-Palacios G; Reyes M; Damian-Matsumura P; Garcia G A; Grillasca I; Lemus A E
CORPORATE SOURCE: Department of Reproductive Biology, National Institute of Medical Sciences and Nutrition S. Zubiran, Vasco de Quiroga 15, Mexico City, C.P. 14000, Mexico.
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (2001 Sep 14) 427 (2) 167-74.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200111
ENTRY DATE: Entered STN: 20010917
Last Updated on STN: 20011105
Entered Medline: 20011101

AB Levonorgestrel (13beta-ethyl-17alpha-ethynyl-17beta-hydroxy-4-gonen-3-one), a potent **contraceptive progestin** stimulates growth and proliferation of cultured breast cancer cells through a receptor-mediated mechanism, even though levonorgestrel does not bind to the oestrogen receptor (ER). To assess whether the oestrogen-like effects induced by this synthetic **progestin** are exerted via its metabolic conversion products, we studied the binding affinity of three A-ring levonorgestrel derivatives to the ER and their capability to transactivate an oestrogen-dependent yeast system co-transfected with the human ER gene and oestrogen responsive elements fused to a beta-**galactosidase** reporter vector. The results demonstrated that the 3beta,5alpha reduced levonorgestrel derivative and to a lesser extent its 3alpha isomer interact with the oestrogen receptor, with a significantly lower relative binding affinity (2.4% and 0.4%, respectively) than that of oestradiol (100%), while levonorgestrel does not. Both levonorgestrel metabolites were able to activate, in a dose-dependent manner, the beta-**galactosidase** reporter gene in the yeast expression system, an effect that was precluded by a steroidal antioestrogen. The oestrogenic potency of levonorgestrel metabolites was significantly lower (750-fold) than that of oestradiol. Furthermore, high doses of 3beta,5alpha levonorgestrel (2.5 mg/day/6 days) induced an increase of oestrogen-dependent **progestin** receptor in the anterior pituitary of castrated rats. The overall data offer a plausible explanation for the weak oestrogenic effects induced by high, non-pharmacological doses of levonorgestrel.

L14 ANSWER 5 OF 27 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-091069 [10] WPIDS
DOC. NO. CPI: C2001-026721
TITLE: New composition for regulating fertility, and for chemoprevention and chemotherapy of cancer, comprises an

antisense oligonucleotide that is complementary to a nucleotide sequence of a follicle-stimulating hormone receptor.

DERWENT CLASS: A96 B04 D16
INVENTOR(S): LABARBERA, A R; WANG, Y; ZHU, C
PATENT ASSIGNEE(S): (UYCI-N) UNIV CINCINNATI
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000073416	A1	20001207	(200110)*	EN	89

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000051379 A 20001218 (200118)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000073416	A1	WO 2000-US13488	20000516
AU 2000051379	A	AU 2000-51379	20000516

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000051379	A	Based on	WO 200073416

PRIORITY APPLN. INFO: US 1999-158612P 19991008; US 1999-136489P 19990528
AN 2001-091069 [10] WPIDS
AB WO 200073416 A UPAB: 20010220
NOVELTY - A composition (C), which comprises at least one antisense oligonucleotide that is complementary to a nucleotide sequence of a follicle-stimulating hormone receptor (FSHR), and that is for regulating hormones of a host, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) regulating the fertility of a host comprising contacting host ovarian cells with a safe and effective amount of (C); and

(2) chemoprevention or chemotherapy in a host comprising contacting host cells with (C).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Hormone modulator; follicle stimulating hormone receptor (FSHR) inhibitor. The antisense oligonucleotide of (C) inhibited the expression of pFSHR protein. Cells that had been transfected with 10 micro M antisense oligonucleotide added directly to the culture medium without lipofectamine exhibited a 13.6 plus or minus 0.8 % (p less than 0.05) decrease in 125I-hFSH binding within 24 h. In 48 h, binding was reduced to 76.0 plus or minus 1.5 % (p less than 0.05). Transfection with lipofectamine and 0.33 micro M antisense oligonucleotide at 0 h caused 76.1 plus or minus 1.3 % (p less than 0.05) reduction in binding within 24 h. The nonsense oligonucleotide did not cause a significant reduction of 125I-hFSH binding with either treatment.

USE - (C) is useful for regulating the hormones of a host. It is

also useful for regulating the fertility and menstrual cycle, and for chemoprevention or chemotherapy (all claimed). It is particularly useful as a chemopreventive or chemotherapy for cancers (e.g. breast, bladder, cervix, lung, liver, ovary, colon, stomach, or especially ovarian cancers), gestational trophoblastic tumors or testicular germ cell tumors. (C) is specifically useful for blocking FSH action on epithelial ovarian cancer cells, which would limit or prevent the progression of the disease. It is useful for preventing estrogen synthesis which is a therapeutic consideration for the prevention and treatment of some cancers or endometriosis. Regulating the fertility and menstrual cycles and chemoprevention or chemotherapy are useful in the management of clinical states of menstrual irregularity, menstrual dysfunction, ovulation pain, primary dysmenorrhea, premenstrual tension syndrome or menopausal dysfunction.

ADVANTAGE - (C) has a high degree of specificity. It does not affect any other cells in the body, unlike estrogens and **progestins**, which affect the brain, skeleton, liver, kidneys or heart.

Dwg.0/5

L14 ANSWER 6 OF 27 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2000413862 MEDLINE
DOCUMENT NUMBER: 20291187 PubMed ID: 10828854
TITLE: The oestrogenic effects of gestodene, a potent **contraceptive progestin**, are mediated by its A-ring reduced metabolites.
AUTHOR: Lemus A E; Zaga V; Santillan R; Garcia G A; Grillasca I; Damian-Matsumura P; Jackson K J; Cooney A J; Larrea F; Perez-Palacios G
CORPORATE SOURCE: Department of Reproductive Biology, Universidad Autonoma Metropolitana-Iztapalapa, Mexico City, Mexico.. ppal@cenids.ssa.gob.mx
SOURCE: JOURNAL OF ENDOCRINOLOGY, (2000 Jun) 165 (3) 693-702. Journal code: 0375363. ISSN: 0022-0795.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000829

AB Gestodene (17 alpha-ethynyl-13 beta-ethyl-17 beta-hydroxy-4, 15-gonadien-3-one) is the most potent synthetic **progestin** currently available and it is widely used as a fertility regulating agent in a number of **contraceptive** formulations because of its high effectiveness, safety and acceptability. The observation that **contraceptive** synthetic **progestins** exert hormone-like effects other than their progestational activities, prompted us to investigate whether gestodene (GSD) administration may induce oestrogenic effects, even though the GSD molecule does not interact with intracellular oestrogen receptors (ER). To assess whether GSD may exert oestrogenic effects through some of its neutral metabolites, a series of experimental studies were undertaken using GSD and three of its A-ring reduced metabolites. Receptor binding studies by displacement analysis confirmed that indeed GSD does not bind to the ER, whereas its 3 beta,5 alpha-tetrahydro reduced derivative (3 beta GSD) interacts with a relative high affinity with the ER. The 3 alpha,5 alpha GSD isomer (3 alpha GSD) also binds to the ER, though to a lesser extent. The ability of the A-ring reduced GSD derivatives to induce oestrogenic actions was evaluated by the use of two different molecular bioassays: (a) transactivation of a yeast

system co-transfected with the human ER alpha (hER alpha) gene and oestrogen responsive elements fused to the beta-**galactosidase** reporter vector and (b) transactivation of the hER alpha-mediated transcription of the chloramphenicol acetyl transferase (CAT) reporter gene in a HeLa cells expression system. The oestrogenic potency of 3 beta GSD was also assessed by its capability to induce oestrogen-dependent **progestin** receptors (PR) in the anterior pituitary of castrated female rats. The results demonstrated that 3 beta GSD and 3 alpha GSD were able to activate, in a dose-dependent manner, the hER alpha-mediated transcription of both the beta-**galactosidase** and the CAT reporter genes in the yeast and HeLa cells expression systems respectively. In both assays the 3 beta derivative of GSD exhibited a significantly greater oestrogenic effect than its 3 alpha isomer, while unchanged GSD and 5 alpha GSD were completely ineffective. Neither 3 beta GSD nor 3 alpha GSD exhibited oestrogen synergistic actions. Interestingly, the pure steroidal anti-oestrogen ICI-182,780 diminished the transactivation induced by 3 beta GSD and 3 alpha GSD in the yeast expression system. Furthermore, administration of 3 beta GSD resulted in a significant increase of oestrogen-dependent PR in the anterior pituitaries of castrated rats in comparison with vehicle-treated animals. The characteristics of the 3 beta GSD-induced PR were identical to those induced by oestradio benzoate. The overall results demonstrate that 3 beta GSD and its 3 alpha isomeric alcohol specifically bind to the ER and possess a weak intrinsic oestrogenic activity, whereas unmodified GSD does not. The data contribute to a better understanding of the GSD mechanism of action and allow the hypothesis to be advanced that the slight oestrogenlike effects attributable to GSD are mediated by its non-phenolic, tetrahydro reduced metabolites.

L14 ANSWER 7 OF 27 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1999-456878 [38] WPIDS
DOC. NO. CPI: C1999-133991
TITLE: Preparation of crystalline form of estradiol used for transdermal delivery formulations for systemic administration in **hormone replacement therapy**, treatment of osteoporosis or **contraception**.
DERWENT CLASS: A96 B01
INVENTOR(S): FARINAS, K C; JAYALAKSHMI, Y; LEE, S M; SONI, P L
PATENT ASSIGNEE(S): (CYGN-N) CYGNUS INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5928666	A	19990727	(199938)*		10

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 5928666	A	Provisional	US 1996-30524P	19961112
			US 1997-968769	19971110

PRIORITY APPLN. INFO: US 1996-30524P 19961112; US 1997-968769 19971110
AN 1999-456878 [38] WPIDS
AB US 5928666 A UPAB: 19990922
NOVELTY - Preparation of crystalline form of estradiol characterized by at

least one diffraction peak with an 2 theta angle of 11.2 deg. plus or minus 0.2 deg. , 12.7 deg. plus or minus 0.2 deg. , 17.4 plus or minus 0.2 deg. or 19.6 plus or minus 0.2 deg. (Crystal X) is new.

DETAILED DESCRIPTION - Preparation of crystalline form of estradiol comprises:

(1) preparing a supersaturated solution of estradiol hemihydrate crystals in an adhesive and solvent;

(2) removing the solvent;

(3) heating the suspension to a temperature sufficient to dissolve estradiol hemihydrate crystals in adhesive; and

(4) transferring the suspension to conditions in which supersaturation ratio is at least 12.

ACTIVITY - Osteopathic; **contraceptive**.

MECHANISM OF ACTION - Estrogenic.

USE - Used to produce a crystalline form of estradiol for incorporation into pharmaceutical formulations (claimed) for systemic administration of estradiol in **hormone replacement therapy**, for treatment of osteoporosis or for **contraceptive** applications.

ADVANTAGE - Produces a stable, crystalline form of estradiol distinguishable from prior art crystalline structures through its diffraction pattern and having greater **solubility** and thermodynamic activity suitable for incorporation into pharmaceutical formulations.

Dwg.0/1

L14 ANSWER 8 OF 27 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1998-531514 [45] WPIDS
DOC. NO. CPI: C1998-159386
TITLE: Treatment of climacteric symptoms in a male or female - by administration of nitric oxide synthase substrate and/or nitric oxide donor, partial oestrogen antagonist and optionally **progestin**.
DERWENT CLASS: B05
INVENTOR(S): CHWALISZ, K; GARFIELD, R E; HEGELE-HARTUNG, C
PATENT ASSIGNEE(S): (SCHD) SCHERING AG; (TEXA) UNIV TEXAS SYSTEM
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9840076	A1	19980917	(199845)*	EN	27

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW

AU 9866942 A 19980929 (199906)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9840076	A1	WO 1998-US4586	19980310
AU 9866942	A	AU 1998-66942	19980310

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9866942 A Based on WO 9840076

PRIORITY APPLN. INFO: US 1997-812910 19970310
AN 1998-531514 [45] WPIDS
AB WO 9840076 A UPAB: 19981111
A method of treating climacterium (climacteric symptoms) in a male mammal or a non-pregnant female involves administration of (a) a nitric oxide synthase substrate (NOSS) and/or a nitric oxide donor (NOD), (b) a partial estrogen antagonist and (c) optionally a **progestin**. Also claimed is a pharmaceutical composition comprising (a), (b), (c) and an **excipient**.

USE - The treatment is especially used in human females suffering menopausal symptoms or in need of **hormone replacement therapy**; or in human males. Symptoms to be treated include hot flushes, abnormal clotting patterns, uro-genital discomfort and increased incidence of cardiovascular diseases in menopausal or post-menopausal women; or increased risk of cardiovascular disease in ageing men.

ADVANTAGE - The combined therapy is more effective than the individual drugs. The effect is probably due to beneficial (e.g. cardio-protective) effects of NO released from blood vessels.
Dwg.0/0

L14 ANSWER 9 OF 27 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1996-395002 [40] WPIDS
DOC. NO. CPI: C1996-124306
TITLE: New 1-(4-(heterocyclic-alkoxy)phenoxy)-2-phenyl-naphthalene cpds. - useful for alleviating post-menopausal syndrome by inhibiting side effects associated with hormone therapy.
DERWENT CLASS: B03 B05
INVENTOR(S): PALKOWITZ, A D
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI; (PALK-I) PALKOWITZ A D
COUNTRY COUNT: 38
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 729951	A1	19960904	(199640)*	EN	25
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
CZ 9600581	A3	19960911	(199643)		
NO 9600772	A	19960829	(199644)		
FI 9600889	A	19960829	(199646)		
AU 9645732	A	19960905	(199647)		
NZ 286072	A	19961029	(199648)		
US 5567712	A	19961022	(199648)		14
CA 2170337	A	19960829	(199651)		
JP 08268881	A	19961015	(199651)		18
US 5574190	A	19961112	(199651)		12
ZA 9601291	A	19971029	(199749)		50
CN 1137525	A	19961211	(199805)		
BR 9600821	A	19971223	(199806)		
MX 9600743	A1	19970201	(199818)		
AU 694837	B	19980730	(199842)		
HU 9600448	A2	19980928	(199846)		
TW 349946	A	19990111	(199923)		
EP 729951	B1	19990602	(199926)	EN	
R: AL AT BE CH DE DK ES FR GB GR IE IT LI LT LU LV NL PT SE SI					
SG 55098	A1	19981221	(199929)		
DE 69602638	E	19990708	(199933)		

NO 305833	B1	19990802	(199937)
ES 2132841	T3	19990816	(199939)
US 5998401	A	19991207	(200004)
IL 128533	A	20000601	(200045)
CN 1261534	A	20000802	(200058)
CZ 288213	B6	20010516	(200132)
RU 2167849	C2	20010527	(200140)
US 6268361	B1	20010731	(200146)
IL 117168	A	20011125	(200215)
MX 197981	B	20000809	(200216)
US 6355632	B1	20020312	(200221)
PH 32046	A	19990602	(200263)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 729951	A1		EP 1996-300877	19960209
CZ 9600581	A3		CZ 1996-581	19960226
NO 9600772	A		NO 1996-772	19960226
FI 9600889	A		FI 1996-889	19960226
AU 9645732	A		AU 1996-45732	19960226
NZ 286072	A		NZ 1996-286072	19960226
US 5567712	A	Div ex	US 1995-395950	19950228
			US 1995-469971	19950606
CA 2170337	A		CA 1996-2170337	19960226
JP 08268881	A		JP 1996-37970	19960226
US 5574190	A	Div ex	US 1995-395950	19950228
			US 1995-465844	19950606
ZA 9601291	A		ZA 1996-1291	19960219
CN 1137525	A		CN 1996-105727	19960226
BR 9600821	A		BR 1996-821	19960226
MX 9600743	A1		MX 1996-743	19960226
AU 694837	B		AU 1996-45732	19960226
HU 9600448	A2		HU 1996-448	19960226
TW 349946	A		TW 1996-101903	19960215
SG 55098	A1		SG 1996-6121	19960227
DE 69602638	E		DE 1996-602638	19960209
			EP 1996-300877	19960209
NO 305833	B1		NO 1996-772	19960226
ES 2132841	T3		EP 1996-300877	19960209
US 5998401	A		US 1995-395950	19950228
IL 128533	A	Div ex	IL 1996-117168	19960219
			IL 1996-128533	19960219
CN 1261534	A	Div ex	CN 1996-105727	19960226
			CN 1999-123572	19960226
CZ 288213	B6		CZ 1996-581	19960226
RU 2167849	C2		RU 1996-103632	19960226
US 6268361	B1	Div ex	US 1995-395950	19950228
			US 1995-466954	19950606
IL 117168	A		IL 1996-117168	19960219
MX 197981	B		MX 1996-743	19960226
US 6355632	B1	Div ex	US 1995-395950	19950228
		Cont of	US 1995-466954	19950606
			US 2000-563282	20000503
PH 32046	A		PH 1996-52436	19960226

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 694837	B	Previous Publ.	AU 9645732
DE 69602638	E	Based on	EP 729951
NO 305833	B1	Previous Publ.	NO 9600772
ES 2132841	T3	Based on	EP 729951
IL 128533	A	Div ex	IL 117168
CZ 288213	B6	Previous Publ.	CZ 9600581
US 6355632	B1	Div ex	US 5998401
		Cont of	US 6268361

PRIORITY APPLN. INFO: US 1995-395950 19950228; US 1995-469971 19950606; US 1995-465844 19950606; US 1995-466954 19950606; US 2000-563282 20000503

AN 1996-395002 [40] WPIDS

AB EP 729951 A UPAB: 19961007

((Heterocyclic-alkoxy)-phenoxy)-naphthalene cpds. of formula (I) and their salts are new. (I); R1 = H, OH, 1-4C alkoxy, OCOC6H5, 1-6C alkylcarbonyloxy or 2-6C alkylsulphonyloxy; R2 = as for R1, or halo; R3 = 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidino, 4-morpholino, dimethylamino, diethylamino, diisopropylamino or 1-hexamethyleneimino; n = 2 or 3.

Also claimed are intermediates of formula (II) and their salts. R' = H or OR5; R'' = H, halo or OR6; R5, R6 = OH protecting gp.; R4 = OH or CHO.

Also claimed is a formulation contg. (I) and opt. estrogen or **progestin**, associated with one or more carriers, **excipients** or diluents.

USE - (I) is useful in the treatment of symptoms associated with postmenopausal syndrome, (esp. osteoporosis, cardiovascular disease, hyperlipidaemia or hormonally-dependent cancer), and as an agent to inhibit uterine fibroid disease, endometriosis, aortal smooth muscle cell proliferation or restenosis (claimed). (I) inhibit side effects of oestrogen and **progestin**.

Dosage is 5-600 (pref. 15-80) mg/day.

ADVANTAGE - (I) prevents the side effects of **hormone replacement therapy**, so avoiding costly and potentially complicating surgical procedures.

Dwg.0/0

ABEQ US 5567712 A UPAB: 19961202

A method for inhibiting endometriosis comprising administering to a woman in need of such treatment an effective amount of a compound of compound of formula (I) wherein

R1 is -H, -OH, -O(C1-C4 alkyl), -OCOC6H5, -OCO(C1-C6 alkyl), or -OSO2(C2-C6 alkyl);

R2 is -H, -OH, -O(C1-C4 alkyl), -OCOC6H5, -OCO(C1-C6 alkyl), -OSO2(C2-C6 alkyl), or halo;

R3 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidino, 4-morpholino, dimethylamino, diethylamino, diisopropylamino, or 1-hexamethyleneimino; and

n is 2 or 3; or a pharmaceutically acceptable salt thereof.

Dwg.0/0

ABEQ US 5574190 A UPAB: 19961219

A compound of formula (II) wherein R1a is -H or -OR5 in which R5 is a hydroxy protecting group; Ra is -H, halo, or -OR6 in which R6 is a hydroxy protecting group; and R4 is -OH or -CHO; or a pharmaceutically acceptable salt thereof.

Dwg.0/0

L14 ANSWER 10 OF 27 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 97092095 MEDLINE

DOCUMENT NUMBER: 97092095 PubMed ID: 8937760
TITLE: Increased levels of several lysosomal enzymes in sera from women using oral **contraceptives**.
AUTHOR: Sanchez-Martin M M; Cabezas-Delamare M J; Cabezas J A
CORPORATE SOURCE: Departamento de Bioquimica y Biologia Molecular, Facultad de Biologia, Salamanca, Spain.. mmario@gugu.usal.es
SOURCE: CLINICA CHIMICA ACTA, (1996 Nov 29) 255 (2) 173-81.
Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 20000303
Entered Medline: 19970227

AB The activities of eight lysosomal enzymes were measured by spectrophotometric/spectrofluorimetric techniques in the blood sera of 19-24 apparently healthy women using an oral **contraceptive** (**progestin** and oestradiol synthetic derivative, desogestrel+ethinyloestradiol) in comparison with 15-16 non-pregnant women not using **contraceptives** (controls), in a randomised, double-blind, controlled study. beta-Glucuronidase and arylesterase showed statistically increased activities (P < or = 0.05) in the experimental group in comparison to the controls. No significant differences were found for the remaining enzymes assayed (beta-N-acetylhexosaminidase, alpha-L-fucosidase, alpha-mannosidase, beta-**galactosidase**, alpha-**galactosidase** and acid phosphatase). Similar results were obtained when the **contraceptive** formed by the combination of levonorgestrel and ethinyloestradiol was used by an experimental group of eight healthy women. These results suggest that the significant increases in the above-mentioned activities might be the physiological response of the organism (through catabolic processes catalysed by lysosomal enzymes) to the administration of exogenous synthetic compounds, such as the oral **contraceptives** used.

L14 ANSWER 11 OF 27 MEDLINE
ACCESSION NUMBER: 2002554602 MEDLINE
DOCUMENT NUMBER: 21755930 PubMed ID: 12287157
TITLE: **Progestin**-only methods safe during lactation.
AUTHOR: Anonymous
SOURCE: Network, (1993 Oct) 14 (2) 32-3.
Journal code: 9875754. ISSN: 0093-3341.
Report No.: PIP-091467; POP-00228458.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Population
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 20021101
Last Updated on STN: 20021101
Entered Medline: 19940705

AB About 90% of women give their infants breast milk. It is the best nutrition for them and prevents infection. Lactation protects against pregnancy for at least 6 months. After 6 months, breast-feeding mothers need a reliable **contraceptive** method. Their 1st choice should be nonhormonal **contraception**, such as IUDs, barrier methods, spermicides, and sterilization. Some women want hormonal methods because

they are convenient and effective. **Progestin**-only methods are the preferable hormonal **contraception** since they are safe for mother and infant. They include the **progestin**-only pill; the subdermal implant, Norplant; and injectables with norethisterone enanthate and depot-medroxyprogesterone acetate (DMPA). The mechanisms by which **progestin**-only methods prevent pregnancy are thickening of the cervical mucus, trimming the uterine lining, and, sometimes, suppressing ovulation. Breast-feeding and family planning specialists do not agree on when lactating women should begin using the **progestin**-only methods. IPPF says they can start as early as 6 weeks' postpartum. Other specialist groups claim that women can wait up to 4 months' postpartum. A study in Argentina reveals no harm to infants when mothers began **progestin**-only methods at 1 week postpartum. The initial higher dose of injectables is a special concern. In addition to timing, providers and clients must also consider the feasibility of returning to a clinic for **contraception**. A Swedish study shows no detectable **progestin** in the blood of infants whose mothers use the **progestin**-only pill, suggesting that infants metabolize the **progestin**. **Progestin**-only methods do not reduce breast milk production and may even increase it. DMPA may affect the concentration of **lactose**, calories, and nitrogen in breast milk, but these changes should not be a problem in areas where women are adequately nourished. Further research of DMPA and breast milk component levels in populations with less than ideal nutrition levels is needed. **Progestins** appear to cause no longterm harmful effects.

L14 ANSWER 12 OF 27 MEDLINE
ACCESSION NUMBER: 92398320 MEDLINE
DOCUMENT NUMBER: 92398320 PubMed ID: 1381897
TITLE: Concentration of fat, protein, **lactose** and energy in milk of mothers using hormonal **contraceptives**.
AUTHOR: Costa T H; Dorea J G
CORPORATE SOURCE: Department of Nutrition, Faculty of Health Sciences, University of Brasilia, Brazil.
SOURCE: ANNALS OF TROPICAL PAEDIATRICS, (1992) 12 (2) 203-9.
Journal code: 8210625. ISSN: 0272-4936.
Report No.: PIP-077798; POP-00217917.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19921023
Last Updated on STN: 20021101
Entered Medline: 19921015

AB Energy, protein, **lactose** and fat were studied in the milk of mothers who were using different types of **contraceptives**. One hundred and eleven mothers made up the following groups. C: control (barrier and natural methods, or sterilization), n = 22; combined pill: LDP (low dose pill (levonorgestrel 0.15 mg + ethinylestradiol 0.03 mg)), n = 12 and MDP (medium dose pill (levonorgestrel 0.25 mg + ethinylestradiol 0.05 mg)), n = 13; MP (minipill (norethindrone 0.35 mg)), n = 37; DMPA (injectable progesterone (depot medroxiprogesterone acetate 150 mg)), n = 17; and IUD (plastic or copper intrauterine device), n = 10. The mean stages of lactation were, respectively, 15, 17, 5, 9, 5 and 9 weeks. The mean duration of observation for the study groups ranged from 2 to 4 weeks. Milk samples were collected before and after initiation of treatment (mean = 20 days; range = 14-103 days). The stage of lactation and the interval of nursing before sampling were recorded so that statistical account could be taken of these uncontrollable sources of

variability. When incorporated as covariates, they showed that no significant differences existed between the groups tested, either before or after treatment.
Researchers compared data on 22 women using either a barrier method or a natural family planning method or had undergone female sterilization (controls) with data on 89 women using either a low dose combined oral **contraceptive** (OC), a medium dose combined OC, a low dose **progestin** only OC, the injectable Depo-Provera, or an IUD to examine the hormonal **contraceptives'** effects on the concentration of total protein, lipids, **lactose**, and energy in human milk. They recruited the women from private and public family planning clinics in Brasilia, Brazil between 1984 and 1987. The mean stages of lactation were 15 weeks for controls, 17 weeks for women using the combined low dose OC, 5 weeks for those using the combined medium dose OC, 5 weeks for those using the combined medium dose OC, 9 weeks for those using the low dose **progestin** only OC, 5 weeks for those using Depo-Provera, and 9 weeks for those using the IUD. Almost all the concentrations of total protein, lipids, **lactose**, and energy both before and after **contraceptive** therapy fell within the range for healthy women. The mean value of total protein in women using Depo-Provera was the only value higher than that range. The low dose OC was associated with a considerable increase in fat (3 g/dL vs. 4.8 g/dL; p=.035). Women taking the medium dose OC experienced a significant decrease in **lactose** (6.8 g/dL vs. 7.25 g.dL; p=.004). The time between last nursing and milk sample collection (nursing interval) caused considerable variation in fat (p=.03) and total energy (p=.02) in those samples collected before **contraceptive** therapy. When the researchers adjusted the data for stage of lactation and nursing interval from all 6 groups, the **contraceptives** had no significant effect on total protein, lipids, **lactose**, and energy.

L14 ANSWER 13 OF 27 MEDLINE
ACCESSION NUMBER: 92053247 MEDLINE
DOCUMENT NUMBER: 92053247 PubMed ID: 1947224
TITLE: A review of the use of progestogen-only minipills for **contraception** during lactation.
AUTHOR: Fraser I S
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, University of Sydney, NSW, Australia.
SOURCE: REPRODUCTION, FERTILITY, AND DEVELOPMENT, (1991) 3 (3) 245-54. Ref: 48
Journal code: 8907465. ISSN: 1031-3613.
Report No.: PIP-068672; POP-00205764.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 20021101
Entered Medline: 19911220

AB Progestogen-only minipills and other systems for releasing low doses of progestogens alone are widely used for **contraception** in breast-feeding women around the world. There is good evidence to confirm their acceptability and their lack of effect on milk production, neonatal growth and early development. In contrast, combined oral **contraceptives** frequently decrease milk production, and may produce minor changes in milk composition. However, even combined oral

contraceptives do not appear to produce adverse effects on neonatal well-being and development, although minor reductions in initial growth rate may sometimes occur. Progestogen-only methods may also produce subtle changes in milk composition, although less than combined oral **contraceptives**. Steroids are transferred from plasma into milk in small quantities, but the amounts are usually very low or insufficient to allow detection in the infants using present-day assays. There has been theoretical concern that these tiny amounts of steroids might affect neonatal reproductive development, but this appears to be unwarranted. Progestogen-only methods are being widely used for post-partum **contraception**, and they appear to have particular advantages in this situation. They also have few disadvantages; a theoretical concern about a possible effect on later reproductive or sexual development has no evidence to support it. The present licensing situation in Australia, which lists lactation as a relative contraindication to progestogen-only **contraceptive** use, causes real concern to potential users and appears to lead to frequent errors in compliance.
A review of the literature revealed no justification for the identification in Australia of lactation as a relative contraindication for use of progestogen-only **contraceptives**. The patient information leaflet expresses concern about the effect on the growing infant of the small amounts of hormone that are found in human milk and possible reductions in milk supply. However, several studies have documented that progestogen-only **contraceptive** systems do not decrease--and in many cases actually increase--milk volume. In addition, the marginal changes in breast milk composition found in users of combined oral **contraceptives** have not been recorded in progestogen-only minipills. A study conducted in India found no significant differences between women treated with levonorgestrel and controls in terms of milk volume, total nitrogen, non-protein nitrogen, and important proteins and **lactose**. Concentrations of levonorgestrel in human milk are lower than those of norethindrone because of the lower oral dosage of the former. Moreover, even if a total 40 ng of norethindrone is ingested during breastfeeding, the amount of the hormone in an infant's bloodstream would be undetectable. Finally, there has been no published evidence of any adverse effect through adolescence of progestogens on physical and mental growth; in fact, some studies have recorded increased neonatal weight gain in infants of mothers who use oral or injectable progestogen **contraceptives**.

L14 ANSWER 14 OF 27 MEDLINE
ACCESSION NUMBER: 86222812 MEDLINE
DOCUMENT NUMBER: 86222812 PubMed ID: 3086241
TITLE: Antacid does not reduce the bioavailability of oral **contraceptive** steroids in women.
AUTHOR: Joshi J V; Sankolli G M; Shah R S; Joshi U M
SOURCE: INTERNATIONAL JOURNAL OF CLINICAL PHARMACOLOGY, THERAPY, AND TOXICOLOGY, (1986 Apr) 24 (4) 192-5.
Journal code: 8003415. ISSN: 0174-4879.
Report No.: PIP-042997; POP-00169095.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 198606
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 20021101
Entered Medline: 19860627
AB The bioavailability of **contraceptive** steroids was studied in 12 women who were given an antacid and a **contraceptive** pill

simultaneously. They were given a single pill containing ethinyl estradiol (EE2) 30 micrograms in combination with either norethisterone (NET) acetate 1 mg (n = 6), or levonorgestrel (LNg) 150 micrograms, (n = 6). Blood samples were collected up to 24 hours. Four weeks later the same pill was administered along with a single tablet of antacid (magnesium trisilicate 0.5 g and dried aluminum hydroxide 0.25 g) and blood samples were collected as before. Serum levels of NET, LNg and EE2 were measured by radioimmunoassay. No effect of antacid administration on bioavailability of any **contraceptive** steroid was observed as judged by peak levels and areas under concentration-time curve (AUC). Incidentally, significantly higher serum concentrations of EE2 were observed when it was administered in combination with NET than with LNg. The possible reasons for this finding are discussed.
The serum levels of both the estrogen and **progestin** in 2 different oral **contraceptives** were analyzed by radioimmunoassay (RIA) for 24 hours after taking a single **contraceptive** pill with or without an antacid. 6 Indian women not taking any other medication took a 30 mcg ethinyl estradiol (EE) and 1 mg norethisterone (NET) pill, and 6 others took a 30 mcg EE with 150 mcg levonorgestrel (LNg) pill at 9 AM. 4 wks later they took the same steroid pill after chewing a tablet of antacid containing magnesium trisilicate .5 g and aluminum hydroxide .25g (Gelusil, Warner). Serum RIA levels and areas under the curves were identical, when each group served as its own control, except that EE levels were significantly higher in the NET combination. The reasons for this discrepancy, whether due to pill **excipients**, radioimmunoassay cross reactions or biological factors such as sex hormone binding globulin activities, were unexplained. Apparently, self-dosing with this antacid will not affect bioavailability of oral **contraceptive** steroids.

L14 ANSWER 15 OF 27 MEDLINE
ACCESSION NUMBER: 83153999 MEDLINE
DOCUMENT NUMBER: 83153999 PubMed ID: 6830939
TITLE: Poly(DL-lactide-co-glycolide)/norethisterone microcapsules: an injectable biodegradable **contraceptive**.
AUTHOR: Beck L R; Pope V Z; Flowers C E Jr; Cowsar D R; Tice T R; Lewis D H; Dunn R L; Moore A B; Gilley R M
SOURCE: BIOLOGY OF REPRODUCTION, (1983 Feb) 28 (1) 186-95.
Journal code: 0207224. ISSN: 0006-3363.
Report No.: PIP-041985; POP-00171562.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 198305
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 20021101
Entered Medline: 19830527

AB Microcapsules made from a biocompatible, biodegradable polymeric **excipient**, poly(DL-lactide-co-glycolide) (DL-PLGA) that contained 22 weight percent (wt %) norethisterone (NET), were prepared by a solvent-evaporation microencapsulation process. The effects of changing both the lactide-to-glycolide ratio of the DL-PLGA and the size of the microcapsules on the rate of NET release and the rate of **excipient** biodegradation were determined in vivo. NET release rates were determined in baboons after injecting the microcapsule formulations intramuscularly. Serum samples obtained at various times following treatment were analyzed for NET, progesterone, and estrogen by radioimmunoassay (RIA). Biodegradation kinetics were determined by injecting NET microcapsules made from radiolabeled DL-PLGA intramuscularly into the hind legs of rats.

Residual radioactivity at the injection site was determined at various times after treatment by combustion analysis of the muscle tissue. Changing the ratio of the comonomers to include more glycolide (DL-lactide:glycolide-96:4, 92:8, 87:13, 74:26) increased the rate of NET release and accelerated the biodegradation of the copolymer **excipient**. Decreasing the size of the microcapsules increased the rate of NET release. On the basis of these studies a NET microcapsule formulation has been identified for clinical testing which releases NET for 3 months and biodegrades completely within 6 months.

L14 ANSWER 16 OF 27 MEDLINE
ACCESSION NUMBER: 81244393 MEDLINE
DOCUMENT NUMBER: 81244393 PubMed ID: 6454819
TITLE: Injectable **contraception**.
AUTHOR: Ratner H
SOURCE: MEDICAL JOURNAL OF AUSTRALIA, (1981 May 30) 1 (11) 598-600.
Journal code: 0400714. ISSN: 0025-729X.
Report No.: PIP-002121; POP-00087274.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 198109
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 20021101
Entered Medline: 19810925

AB Two reports indicate that some women may experience a mild adverse effect on milk yield. Variable effects of DMPA (depot medroxyprogesterone acetate) on breast milk composition have been reported. Different studies have reported increased, unchanged, or decreased milk concentrations or total contents of **lactose**, protein or lipid. Another study has indicated a minor depressive effect on development. Recent evidence suggests that milk concentrations of MPA may be as high as maternal plasma levels and transfer of DMPA may be appreciable. There is some concern that DMPA may have small effects on growth, maturation and subsequent reproductive function of the neonate. Sammour's study reported a 16% decrease in protein count in milk. Another study shows a 48% decrease in protein. Since reduced protein concentrations mean reduced immunoglobulins, the infant's prime protection against early death, it is a disservice to publicize a conclusion stating that progestogens do not adversely affect milk production and composition.

L14 ANSWER 17 OF 27 MEDLINE
ACCESSION NUMBER: 81221739 MEDLINE
DOCUMENT NUMBER: 81221739 PubMed ID: 6787483
TITLE: [Trial of a new spermatocidal agent in suppository form with local disinfectant action].
Indagine su un nuovo spermicida in candelette ad azione disinfettante locale.
AUTHOR: Orzi C; Mazzilli F; Tellini P
SOURCE: MINERVA GINECOLOGICA, (1981 Jan) 33 (1) 113-6.
Journal code: 0400731. ISSN: 0026-4784.
Report No.: PIP-003612; POP-00088898.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 198108
ENTRY DATE: Entered STN: 19900316

Last Updated on STN: 20021101
Entered Medline: 19810827

AB The in vivo spermicidal action of a pharmacological association consisting of 0.080 g of sodium tetraborate decahydrate, 0.075 g lactic acid, 0.020 g 8-hydroxyquinoline sulphate, 0.005 g sodiopropionate, and hydrosoluble **excipient** 1820 g polyethyl englycol in the form of vaginal containers, has been investigated. The study is part of a more general investigation of alternative systems to the use of estro-**progestins**. The experimental scheme applied in the present study provided for the use of this association in 28 volunteer couples who were definitely fertile and during the pre- and postovulatory periods. A normal postcoital test was carried out on each, with samples taken from the posterior fornix and cervical canal using a speculum. The results showed that the preparation possesses profound spermicidal activity and is therefore considered a useful alternative to oral **contraceptives** . To be absolutely safe, however, other **contraceptive** systems should be used simultaneously during ovulation (condom, diaphragm). (author's)

L14 ANSWER 18 OF 27 MEDLINE
ACCESSION NUMBER: 80150735 MEDLINE
DOCUMENT NUMBER: 80150735 PubMed ID: 7361700
TITLE: Effect of oral **contraceptives** on composition and volume of breast milk.
AUTHOR: Lonnerdal B; Forsum E; Hambraeus L
SOURCE: AMERICAN JOURNAL OF CLINICAL NUTRITION, (1980 Apr) 33 (4) 816-24.
Journal code: 0376027. ISSN: 0002-9165.
Report No.: PIP-800503; POP-00076870.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Population
ENTRY MONTH: 198005
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 20021101
Entered Medline: 19800530

AB Nitrogen and protein composition was determined in milk from women using oral **contraceptives** during lactation. Total nitrogen and nonprotein nitrogen as well as **lactose** and the individual milk proteins lactoferrin, alpha-lactalbumin, and serum albumin were analyzed before introduction of oral **contraceptives** and thereafter throughout the lactation period. Twenty-four hour milk volumes were registered by weighing the infant before and after each feeding. The four oral **contraceptives** used consisted of different combinations of d-norgestrel, megestrolacetate, and ethinylestradiol. Significant changes were observed between groups and controls for all parameters studied. However, the changes observed were generally within the physiological variation of normal breast milk. It is suggested that the use of oral **contraceptives** during lactation should be limited.
The present article reports the results of an investigation on the effects of OC (oral **contraception**) on lactation performance and on composition of breast milk. Mothers collaborating to the study were on combined OCs or on **progestin** only OCs. Before and after introduction of OC, nitrogen **lactose**, lactogerrin, alpha-lactabbumin, and serum albumin were analyzed; milk volume was measured by weighing the infant before and after each feeding. Significant changes were found in concentration of total protein and in individual milk protein, the magnitude of changes varying between components

investigated; changes in daily milk volume were also observed. The magnitude of changes were reputed to be still within the normal range, and not to be of nutritional importance. However, negative effects could be observed in marginally or severely malnourished mothers. Use of OC during lactation should be carefully considered, and, if chosen, the lowest possible dose should be given.

L14 ANSWER 19 OF 27 MEDLINE
ACCESSION NUMBER: 2002517638 MEDLINE
DOCUMENT NUMBER: 21708179 PubMed ID: 12335916
TITLE: Effect of the single steroid implant on the quantity and composition of milk in lactating women.
AUTHOR: Pal M N; Singh I; Jalnawalla S F
SOURCE: JOURNAL OF OBSTETRICS AND GYNAECOLOGY OF INDIA, (1979 Jun) 29 (3) 552-6.
Journal code: 0374763. ISSN: 0022-3190.
Report No.: PIP-791830; POP-00052643.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Population
ENTRY MONTH: 198001
ENTRY DATE: Entered STN: 20021101
Last Updated on STN: 20021101
Entered Medline: 19800108

AB A study was undertaken to determine the effects of single steroid implants on the quantity and composition of milk in lactating women. 25 women with well-established lactation in whom the Nor-ethindrone acetate implant with 40 mg of the progestogen was implanted subcutaneously were matched for various characteristics with 25 lactating women who were using conventional **contraceptives**. The women were studied at 6 weeks postpartum and fortnightly for a period of 6 months. A majority of the mothers felt that their milk supply was sufficient and that their infants seemed satisfied; only 2 of the study group had to supplement their milk supply in the 1st 6 months. Concentration of milk protein decreased steadily at every subsequent follow-up in both groups, due to the low intake of protein in this class of women. The values of milk fat and milk **lactose** increased steadily in both groups, more so in the study group. Results of the study indicate that progestogen implant **contraceptives** have no ill effects on the production or quality of milk among lactating mothers.

L14 ANSWER 20 OF 27 MEDLINE
ACCESSION NUMBER: 79174831 MEDLINE
DOCUMENT NUMBER: 79174831 PubMed ID: 374693
TITLE: Essential hormones as carcinogenic hazards.
AUTHOR: Hickey R J; Clelland R C; Bowers E J
SOURCE: JOURNAL OF OCCUPATIONAL MEDICINE, (1979 Apr) 21 (4) 265-8.
Ref: 22
Journal code: 7502807. ISSN: 0096-1736.
Report No.: PIP-795926; POP-00071363.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 197907
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 20021101
Entered Medline: 19790725

AB Recently, the Occupational Safety and Health Administration (OSHA) proposed regulations regarding lists of environmental substances that allegedly pose potential occupational carcinogenic risk. Known carcinogens such as bis(chloromethyl) ether, along with natural substances such as estradiol, estriol, estrone, progesterone, tannic acid, maltose, and **lactose**, were included in the general OSHA list. Clear distinction between true hazards and essential endogenously formed biochemicals was not made. A major reappraisal of the OSHA list is essential. The revised document should indicate the conditions under which various classes of substances constitute human health hazards -- including dosage levels and routes of entry.
The OSHA (Occupational Safety and Health Administration) considers certain substances to be carcinogenic including such hazardous chemicals as benzo(a)pyrene, asbestos, bis(chloromethyl) ether, 2-naphthylamine, and aflatchines B2 and G1 as well as natural substances such as estradiol, estriol, estrone, progesterone, tannic acid, maltose, and **lactose** . The results of the carcinogenic effects of these natural substances is in question because of administered dosage levels, chemical structure of the substances, the route the hormones entered the biological system, and testing done in animals and in vitro. Citing **lactose**, found in milk, and nitrite, found in saliva, as carcinogenics shows a lack of discrimination between authentic carcinogenic hazards and evolved natural chemicals endogenously produced which are essential to survival. It is suggested that OSHA reappraise the substances to indicate the conditions under which substances may be considered a human health hazard including dosages and routes of entry.

L14 ANSWER 21 OF 27 MEDLINE
ACCESSION NUMBER: 77132496 MEDLINE
DOCUMENT NUMBER: 77132496 PubMed ID: 842864
TITLE: Determination of noretisterone in tablets by differential pulse polarography.
AUTHOR: Opheim L N
SOURCE: ANALYTICA CHIMICA ACTA, (1977 Mar) 89 (1) 225-9.
Journal code: 0370534. ISSN: 0003-2670.
Report No.: PIP-775149; POP-00046028.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 197704
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 20021101
Entered Medline: 19770425

AB A rapid differential pulse polarographic method for quantitative determination of norethisterone (NE) in a tablet is described. The procedure involves disintegrating the tablet with a few drops of distilled water inside a 100 ml volumetric flask, addition of 40 ml methanol, addition of 20 ml .2 M tetramethyl ammonium bromide solution, and dilution to the mark with distilled water. 25 ml of the solution are then transferred to a polarographic cell, dissolved air is removed by bubbling nitrogen through the liquid, and the differential pulse polarographic peak is recorded. A 10 ppm standard sample solution, with **excipients** corresponding to 1 tablet, and a blank solution with **excipients** only are both tested in the same manner. The amount of NE can then be calculated as the ratio of the peak currents of the tablet solution to those of the standard solution measured against those of the blank solution. Peak current increases linearly as a function of concentration of NE over the range 2-200 ppm.

L14 ANSWER 22 OF 27 MEDLINE
ACCESSION NUMBER: 75213604 MEDLINE
DOCUMENT NUMBER: 75213604 PubMed ID: 1151688
TITLE: Rapid, sensitive colorimetric method for determination of ethinyl estradiol.
AUTHOR: Eldawy M A; Tawfik A S; Elshabouri S R
SOURCE: JOURNAL OF PHARMACEUTICAL SCIENCES, (1975 Jul) 64 (7) 1221-3.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197511
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19751107

AB A colorimetric procedure, based on the formation of an azo dye by condensation of diazotized 5-chloro-2,4-dinitroaniline with ethinyl estradiol, was developed. An alkaline solution of ethinyl estradiol is reacted with the reagent, and the resulting color is measured at 450 nm. Absorbance versus concentration is linear up to 10 mug/ml; the lower limit of detection is 1 mug/ml under the conditions studied. Replicate analysis showed good agreement, and an average recovery of 99.6 +/- 0.3% was obtained for analyses of synthetic mixtures. Vitamins and minerals likely to be present along with ethinyl estradiol in certain geriatric formulations, as well as ordinary tablet **excipients** and coating materials, do not interfere with the precision of the method or development of the color. The method is applicable to **progestin** -estrogen preparations. Assay results on various single-component as well as **contraceptive** commercial samples are reported.

L14 ANSWER 23 OF 27 MEDLINE
ACCESSION NUMBER: 76084380 MEDLINE
DOCUMENT NUMBER: 76084380 PubMed ID: 1239152
TITLE: Effect of two long acting injectable progestogens on lactation in the human.
AUTHOR: Abdel Kader M M; Abdel Aziz M T; Bahgat M R; Kamal I; Talaat M; Abdallah M; Osman M
SOURCE: ACTA BIOLOGICA ET MEDICA GERMANICA, (1975) 34 (7) 1199-204.
Journal code: 0370276. ISSN: 0001-5318.
Report No.: PIP-752930; POP-00024543.
PUB. COUNTRY: GERMANY, EAST: German Democratic Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 197602
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 20021101
Entered Medline: 19760209

AB The effects of Depoprovera and Deladroxone were studied in humans, on certain milk components as well as on the growth of the nursed infants. Both drugs caused reduction in milk yield. Both drugs caused an increase in the concentration of milk total proteins, however. Depoprovera caused an increase while Deladroxone caused a decrease in the total amount of milk proteins per feed. Depoprovera showed no effect while Deladroxone caused an increase in the concentration of milk lipids; however, both drugs caused reduction in the total amount of milk lipids per feed. Both drugs showed no effect on the concentration of milk **lactose**, but caused reduction in the total amount of milk **lactose** per feed.

The percentage increase in weight of nursed infants was decreased by Depoprovera, but not affected by Deladroxone.
The effects of Depo Provera and Deladroxone, both long-acting inject able **contraceptive** agents, on lactation and infant growth was studied in 76 lactating women. Milk yield was decreased by both drugs, though the concentration of total milk proteins was increased. Depo Provera increased the total amount of milk proteins per feed, while a decrease was observed with Deladroxone. Deladroxone increased the concentration of milk lipids, but Depo Provera had no effect. Nonetheless, both agents reduced the total amount of milk lipids per feed. Concentrations of milk **lactose** were unaffected, but the total amount of milk **lactose** per feed was reduced by both drugs. Depo Provera decreased the rate of infant growth, while Deladroxine had no effect.

L14 ANSWER 24 OF 27 MEDLINE
ACCESSION NUMBER: 75183382 MEDLINE
DOCUMENT NUMBER: 75183382 PubMed ID: 4218958
TITLE: Inhibition by progesterone of the lactogenic effect of prolactin in the pseudopregnant rabbit.
AUTHOR: Assairi L; Delouis C; Gaye P; Houdebine L M; Bousquet M O; Denamur R
SOURCE: BIOCHEMICAL JOURNAL, (1974 Nov) 144 (2) 245-52.
Journal code: 2984726R. ISSN: 0264-6021.
Report No.: PIP-744404; POP-00018661.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 197509
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 20021101
Entered Medline: 19750903
AB The effects of progesterone on **lactose** synthesis activity and changes in mammary gland cells were studied in pseudopregnant rabbits simultaneously treated with prolactin. The injection of progesterone alone on Days 15 and 17 of pseudopregnancy decreased the activity of **lactose** synthetase (LSA) and **galactosyl** transferase (GTA), while the administration of prolactin for 2-4 days increased their activities. Th e simultaneous administration of progesterone and prolactin decreased the increase in LSA observed with prolactin alone by 70% on the 4th day of treatment, and decreased GTA by 30%. Progesterone completely suppressed the polyribosome profile and the ratio of endoplasmic reticulum bound polyribosomes to free polyribosomes induced by prolactin. The increase in RNA content in the mammary gland induced by prolactin was also suppressed by progesterone. The results suggest that progesterone inhibits the lactogenic action of prolactin without interfe ring with its mammogenic role.

L14 ANSWER 25 OF 27 MEDLINE
ACCESSION NUMBER: 74012246 MEDLINE
DOCUMENT NUMBER: 74012246 PubMed ID: 4126857
TITLE: Mammary nodules in dogs during four years' treatment with megestrol acetate or chlormadinone acetate.
AUTHOR: Nelson L W; Weikel J H Jr; Reno F E
SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1973 Oct) 51 (4) 1303-11.
Journal code: 7503089. ISSN: 0027-8874.
Report No.: PIP-731888; POP-00002620.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 197312
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 20021101
Entered Medline: 19731216

AB A 7 year study of megestrol and chlormadinone in female dogs is in progress. This report characterized histopathologically 60 mammary nodules during the first 4 years of the study. 100 purebred female beagles, 6-12 months of age, were randomly assigned to 5 equal groups. One group was used as a control. Oral doses were .01, .10, and .25 mg/kg/day of megestrol acetate in coconut oil in capsules and of chlormadinone acetate .25 mg/kg/day in **lactose** tablets. These doses were 1, 10, and 25 times the projected dose of megestrol for humans and about 25 times the human dose of chlormadinone. After 2 years 4 dogs from each group were necropsied. One high-dose megestrol-treated and 1 chlormadinone-treated dog had benign mixed mammary tumors. Palpable nodules were first observed at 16 months in the chlormadinone-treated dogs, at 18 months in dogs given the high dose megestrol and at 27 months in the dogs treated with middle-dose megestrol. Transitory nodules were found in 4 control dogs after 21 months and in low dose megestrol-treated dogs at 26 months. Of 38 grossly detected nodules evaluated microscopically from the megestrol-treated dogs 27 were nodular hyperplasia, 5 were benign mixed mammary tumors, 3 were ductal dialatations, 1 was a lymph node, 1 was fat necrosis and 1 was the umbilicus. Of 22 nodules from the chlormadinone-treated dogs 12 were nodular hyperplasia, 4 benign mixed mammary tumors, 1 chondromucoid degeneration and 1 adenocarcinoma with widespread metastases. 3 nodules were lymph nodes and 1 other had no mammary tissue. Involutions, regression and sclerosis of many areas of nodular hyperplasia were evident at 4 years. Thus of the 60 nodules evaluated during the first 4 years of the study 50 were non-neoplastic and 10 were neoplastic. It is considered that the 1 adenocarcinoma may have been spontaneous and not a treatment-related neoplasm. A precursor stage through nodular hyperplasia apparently did not occur.

L14 ANSWER 26 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 74105684 EMBASE
DOCUMENT NUMBER: 1974105684
TITLE: [The behavior of the gonadotropins FSH and LH during and after treatment with estrogenic and **progestinic** drugs: Clinical considerations].
IL COMPORTAMENTO DELLE GONADOTROPINE FSH ED LH DURANTE E DOPO TRATTAMENTO CON **ESTROPROGESTINICI** (CONSIDERAZIONI CLINICHE).
AUTHOR: Ramadori P.; Lirosi G.
CORPORATE SOURCE: I Clin. Ostet. Ginecol., Univ. Studi, Roma, Italy
SOURCE: PATOL.CLIN.OSTET.GINEC., (1973) 1/1 (26-34).
CODEN: XXXXXB
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
010 Obstetrics and Gynecology
003 Endocrinology
023 Nuclear Medicine
LANGUAGE: Italian

AB It has been demonstrated that the antigonadotropic effect of estrogenic and **progestinic** preparations is dependent upon the dosage administered. Until a few years ago, only a rebound effect was observed upon suspension of treatment, while more recent literature has increasingly pointed out a persistent hypothalamic inhibition following the discontinuation of such drugs. Clinical manifestations of this

inhibition include amenorrhea or oligomenorrhea with or without associated galactorrhea. Pathophysiologic considerations of this condition have led to the definition of estrogenic and **progestinic** preparations (when administered in adequate doses to produce an antigonadotropic effect) as drugs having a potential inhibiting effect not only upon FSHRF, LHRF and PIF, but also on GHRF and TRF. It may thus be possible to indicate estrogenic and **progestinic** drugs in the treatment of some dysfunctional forms of acromegaly and hyperthyroidism caused by increases of GHRF and TRF, respectively.

L14 ANSWER 27 OF 27 MEDLINE
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TITLE: Oral **contraceptive** steroids: effects on oral tolerance tests of glucose, **galactose**, fructose and ribose.
AUTHOR: Young A K; Yang M G
SOURCE: Nutr Rep Int, (1971 December) 4 (6) 341-50.
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AB The effects of oral **contraceptives** (OCs) on oral tolerance tests of glucose, **galactose**, fructose, and ribose were studied in 11-week-old female rats. 1 group was fed ad libitum a basal grain diet containing norethynodrel and mestranol while a control group was pair-fed with the experimental rats and received only the basal grain diet. Oral sugar tolerance tests were performed after 1 and 4 weeks of steroid treatment. After 1 week of treatment, oral sugar loading indicated that there was no tolerance impairment based on blood serum glucose levels. However, after 4 weeks of treatment, rats administered glucose had impaired tolerances (p less than .01). Blood serum glucose levels were higher (p less than .05) for treated than for control rats after force-feeding of ribose. No impairment or increase in blood glucose levels was seen after administering fructose or **galactose**. Urine samples were obtained from the animals 2 weeks after the initiation of treatment to determine the quantity of urinary sugars after oral loading of the 4 sugars. Quantities of urinary sugar for the 2 groups were similar for samples obtained for 6 hours immediately after the sugar loading. During the subsequent 18 hours the treated rats had significantly greater quantities of urinary glucose than control rats when they were orally loaded with either glucose (p less than .05) or ribose (p less than .01). 8 pairs of the rats were continued on their respective diets for another 28 weeks, when the quantity of carbon dioxide exhaled subsequent to injections of glucose-u-carbon-14 was appreciably higher for pair-fed control rats compared with those fed the 2 steroids. The metabolism of injected ribose to carbon dioxide was faster for treated rats.